UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF OHIO

EASTERN DIVISION

IN RE NATIONAL PRESCRIPTION	MDL 2804
OPIATE LITIGATION	Case No. 17-md-2804
This document relates to:	Hon. Dan Aaron Polster
The County of Summit, Ohio, et al. v. Purdue Pharma L.P., et al., Case No. 18-OP-45090	

Report of David S. Egilman MD, MPH

March 25, 2019

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2 BACKGROUND AND QUALIFICATIONS

My name is Dr. David Egilman. I am a medical doctor and Clinical Professor of Family Medicine at Brown University. I am board certified in Internal Medicine and Preventive-Occupational Medicine. My *curriculum vitae* [Egilman CV hereto attached as **Exhibit A.1**] sets forth more fully my qualifications.

I received a Bachelor of Science degree in Molecular Biology and a degree in Medicine at Brown University. [Egilman CV at 1] I then completed my three year residency in internal medicine at the University of Rochester. [Egilman CV at 1] I helped start a program focused on women's health. I completed NIH's three-year Epidemiology Training Program. [Egilman CV at 1-2] The first year of this program involved training at the Harvard School of Public Health (HSPH), where I was awarded a Master's Degree in Public Health. [Egilman CV at 1-2] At Harvard, I studied industrial hygiene and toxicology; epidemiology; statistics; occupational medicine and law; public policy with respect to occupational and environmental hazards; areas that relate to the specialty of preventive medicine, including education, product design changes and substitution; warnings and risk communication, including regulatory approaches to control; the tort system; environmental law; Food and Drug Administration (FDA) and OSHA law; and the Consumer Product Safety Commission (CPSC). One course that I completed during the program covering various legal and regulatory approaches to control of health hazards was a joint course offered by the Harvard Law School, the Harvard School of Public Health, and the MIT Business School. I spent the second two years of the National Institutes of Health (NIH) Epidemiology Training Program at NIOSH. As part of my assignment I received the training in epidemiology and surveillance provided by the Centers for Disease Control to Epidemic Intelligence Service officers. At NIOSH, I received training in the law as it applied to NIOSH and OSHA medical officers. I was responsible for implementing parts of the OSHA Act relevant to investigation of worker health. I received training in risk communication and warnings at NIOSH. At NIOSH, I received training in industrial hygiene techniques, conduct of epidemiologic studies, and risk analysis -- particularly as it applied to carcinogens and dose assessment. I designed implemented small and large epidemiological studies. I participated in industrial hygiene sampling and became familiar with industrial hygiene monitoring for asbestos and other toxic exposures. While at NIOSH, I completed the NIOSH residency in occupational medicine in 1984. [Egilman CV at 1] At NIOSH I was a uniformed officer of the U.S. Public Health Service. While at NIOSH, my responsibilities included education of workers, employers and members of the public regarding health hazards. I provided this information through a variety of vehicles, including written reports, conferences, mass meetings and face-to-face conversations. NIOSH and the CDC provided training on the mechanisms of effective communication. I completed a third residency in preventive medicine in 1993. [Egilman CV at 1]

Occupational Medicine is the branch of medicine that deals with the prevention and treatment of diseases and injuries that occur as a result of exposure to chemical substances. This specialty deals with the toxicological effects of exposures to chemical substances on the body. The fundamental aspect of this specialty is the determination of which exposures cause disease, and how they do so. My educational and professional background, training

at HSPH and NIOSH, and teaching and publications provide the basis of my expertise in warnings.

I have extensively studied the role of warnings in preventing illnesses and the current and historical techniques for providing warnings. I have published two chapters in the major textbook relating to warning and risk communication. [Egilman CV at 13: Chapter Two "A Brief History of Warnings," and " Consider The Source: Warnings And Anti-Warnings In The Tobacco, Automobile, Beryllium, And Pharmaceutical Industries" in Wogalter Ed., Warnings and Risk Communication]

My first chapter in the book on Warnings and Risk Communication, (the first full chapter in the book) dealt with the history of warnings; the second addressed the adverse effects of marketing on public health, focusing particularly on false reassurance given by product manufacturers to consumers. Both chapters dealt with issues that related to FDA regulatory authority. Some of my publications have dealt with FDA regulations and I cover FDA-related issues in my course. [Egilman CV at 2, 13, & 19]

I also ran a clinic for 12-13 years, treating patients and consulting in occupational medicine for large and small companies. I treated patients with pain from cancer and chronic non-malignant pain and at times prescribed opioids in my practice. [Egilman IMS Data hereto attached as **Exhibit A.2**]

I am licensed to practice medicine in Massachusetts, Rhode Island, and Mississippi. I have published over 100 papers, including 50 original publications in peer-reviewed journals and 78 presentations. I have authored peer-reviewed publications on epidemiology and causation; regulatory science; warnings, anti-warnings, and risk communication; the development of the corporate, medical and scientific communities' knowledge of the health hazards; and corporate influence on science and regulation.

The Asbestos Disease Awareness Organization (ADAO) awarded me the Irving Selikoff Lifetime Achievement Award for my academic contributions to the prevention of asbestos disease. [Egilman CV at 3]

I have taught several courses at Brown University, including the Development of Medical and Scientific Knowledge in the 20th Century; and Science and Power: A Bioethical Inquiry, and currently teach a course in the Brown School of Public Health called, "Science and Power – The Corruption of Public Health." This course deals specifically with the issues outlined in this report: the history of the development of knowledge regarding the health hazards; FDA regulations; warnings and risk communication, including corporate knowledge of health effects of products; the history of the development of government regulations on occupational, consumer and environmental safety; and the history of the development of contemporaneous appropriate public health responses to information regarding the adverse health effects of products on users, including education of product users and product redesign (state of the art). In my course, I compare the medical and scientific information available to the companies with that available to the medical and scientific community.

I have also published on these topics. I have also taught a two-year course for medical students that covered medical ethics, community approaches to public health, and health education.

I served, for over 10 years, as a preceptor to residents in Family Medicine and medical students, supervising the care of patients. I served for 9 years as the Editor in Chief of a major journal: The International Journal of Occupational & Environmental Health. [Egilman CV at 2]

On two occasions I testified before congressional sub-committees on the issues relating to informed consent and corporate responsibility to inform members of the public about health hazards. My testimony concerned the history of informed consent, warnings, and research ethics. In addition, I have published two papers on the topic of the history of the development of informed consent. I was a board member of Citizens for Responsible Care in Research from 1997- 2009. I am currently a board member of The Alliance for Human Research Protection (AHRP). These non-governmental organizations (NGO) deal with the ethical conduct of research.

I have reviewed the history of warnings from the published literature, and from internal corporate documents and organizational documents. I presented several papers on warnings. I teach about warnings at Brown University, including FDA drug-related warnings. I testified before Congress on the history and development of informed consent, as well as on current informed consent practices. I have been accepted as an expert by the court in Keenan v. Parke-Davis et al. PC 84-1667 (Rhode Island) on the issue of warnings and FDA policy. I have also been accepted as a witness on issues that relate to FDA warning policy in the case of Vassallo v. Baxter Healthcare Corporation, 428 Mass. 1 (1998). My affidavit on medical epistemology was cited by the court. I have reviewed corporate documents specifically addressing warning practices throughout this century. I have studied the efficacy of warnings.

Along with my colleague, Susanna Bohme, I co-authored two chapters in a textbook on the history of warnings: Egilman D.S., Bohme S.R. “A Brief History of Warnings” and “Consider the Source: Warnings and Anti-Warnings in the Tobacco Beryllium, Automobile and Pharmaceutical Industries,” Handbook of Warnings, ed. Michael Wogalter Mahwah, NJ: Lawrence Erlbaum Associates, 2006. In November of 2004, I presented a lecture at the American Public Health Association Conference entitled, “Occupational Warnings: Protecting People or Protecting Profit?” In addition, in July of 2004 at the Center for Science in the Public Interest (CSPI) conference, I presented a lecture on “The Suppression of Science: How Corporate Interests Hide the Truth.” In this talk, I spoke of the need to adequately warn doctors and the public about the health risks of exposure to products, about FDA regulations, and about corporate codes of conduct and ethical standards.

I have presented at the annual American Public Health Association conference off-label marketing and hiding addiction risks. (Egilman DS and Falender J. OxyContin: How Profits Took Priority over Public Health. APHA, Nov 2004.) In February 2013, I presented to the FDA about OxyContin’s 12-hour dosing regimen as a contributing cause of opioid addiction. [FDA Presentation Slides and Transcript hereto attached as **Exhibit A.3 and**

Exhibit A.4] I have authored a number of articles and presentations pertaining to medical and business warnings issues. (See attached CV for complete list of publications and presentations.)

- Writings and presentations explicitly dealing with warnings and disclosure in business and scientific research and publishing:
    - Angell, M et al. Letter to the Editor [Journal Should Strengthen Conflict of Interest Disclosure Policy] Nature Neuroscience 6: 10, October 2003.
    - Egilman, D.S., Ehrle, L.H. Handling Conflicts of Interest between Industry and Academia. JAMA 289, June 25 2003: 3240.
    - Egilman, D., Hornblum, A., Letter to the Editor: Guinea Pigs Behind Bars, The Boston Globe, Monday, November 29, 1999.
    - Egilman, D., Wallace, W., Stubbs, C., and Mora-Corrasco, F. "Ethical Aerobics: ACHRE's Flight from Responsibility." Accountability in Research Vol. 6, pp. 15-61, 1998.
    - Egilman, D., Reinert, A.: What Is Informed Consent? Washington Post, January 14, 1994: P 24.
    - Egilman, D., Ethics of Mandatory Masturbation (letter), JOM, 30;12:992, December 1988.
    - Egilman, D.S., Written Testimony submitted to the US Senate Subcommittee on Antitrust, Competition Policy and Consumer Rights Hearing, "Hospital Group Purchasing: Has the Market Become More Open to Competition?" July 16, 2003.
    - Egilman, David: Oral Testimony Before the President's Advisory Committee on Human Radiation Experiments, July 17, 1995.
    - Egilman, David: Oral Testimony Before the President's Advisory Committee on Human Radiation Experiments, February 1995.
    - Egilman, D., Wallace, W., Stubbs, C., and Mora-Corrasco, F. "A Little Too Much of the Buchenwald Touch? Military Radiation Research at the University of Cincinnati, 1960-1972." Accountability in Research Vol. 6, pp. 63-102, 1998.
    - Egilman, David: International Health Work: First Do No Harm, Family Medicine Grand Rounds, Memorial Hospital of Rhode Island, Feb. 1991.
    - Bailar JC, Ballal SG, Boback M, Castleman B, Heng LC, Cherniack M, Christiani D, Cicolella A, Fernandez de D'Pool J, Egilman DS, et al. (Special Contributions) FIOH-sponsored Newsletter Misrepresents Asbestos Hazards in Zimbabwe. Int J Occup Environ Health 12(3):254-258, Jul-Sept 2006.
    - Egilman DS. Ford, General Motors, Chrysler, Asbestos and a "Sane Appreciation of the Risks" (Editorial). Int J Occup Environ Health 15(1):109-110, Jan-Mar 2009.
    - Egilman DS and Bohme SR. Vioxx Marketing: Merck's Failure to Warn. International Ergonomics Association 2006 Conference Proceedings.

  - Bohme SR and Egilman DS. Pharmaceutical Warnings and "Direct to Consumer" Marketing. International Ergonomics Association 2006 Conference Proceedings.
  - Bohme SR and Egilman DS. Occupational Warnings: Protecting People or Protecting Profit. APHA, Nov 2004.
  - Egilman DS. Panel Member: From Practice to Science: How Application Guides Warning Research. International Ergonomics Association Conference, Jul 2006.
- Other writings and presentations, considering issues relevant to the fields of medical and business practices, including industry influence on research, attorney misconduct in procuring clients, and marketing of products that injure workers and/or consumers:
  - Egilman, D.S., Fehnel, C., Bohme, S.R. Exposing the "Myth" of ABC: A Critique of the Canadian Asbestos Mining Industry-McGill Chrysotile Studies. Amer J Ind Med 44:5, 2003.
  - Egilman, D.S., Bagley, S., Biklen, M., Golub, A.S., Bohme S.R. The Beryllium "Double Standard" Standard. International Journal of Health Services 33:4, 2003.
  - Egilman, D.S., Bagley, S., Connolly, S., Letter to the Editor: Anything But Beryllium: The Beryllium Industry's Corruption of Safety Information, Am. J. Ind. Med., 42:3, September 2002.
  - Egilman, D.S., Asbestos Screenings, Am. J. Ind. Med., 42:2, August 2002.
  - Egilman, D., Walta, M., Letter to the Editor: Breast Implant Verdicts Resulted From Corporate Misconduct and Legitimate Science, Am. J. Pub. H., 89:11 1763-1764, November 1999.
  - Egilman, D., Hom, C., Commentary: Corruption of the Medical Literature: A Second Visit, Am. J. Ind. Med., 34:4 401-404, October 1998.
  - Egilman, D., Wallace, W., Hom, C., W. R. Grace Corporate Corruption of the Medical Literature, Accountability in Research Vol. 6, pp.127-147, 1998.
  - Durand, K. and Egilman, D., Possible Corruption Of IH Literature By DuPont: The Imron Respirator Studies, Am Ind. Hyg.. Assoc. J. 56:817-825, August 1995.
  - Egilman, D., Reinert, A.: The Origin and Development of the Asbestos Threshold Limit Value: Scientific indifference and corporate influence. Int. J. Health Serv. 25:667-696, 1995.
  - Egilman, D., Hardy, HL: Manipulation of Early Animal Research on Asbestos Cancer (letter). Am. J. Ind. Med. 24:787-791.1993.
  - Egilman, D., The emperor has no clothes: TLVs and Corporate influence, Am Ind. Hyg. Assoc. J., 187-188, March 1990.
  - Egilman, D.S., Evidence of Continued Corruption of the Epidemiological Literature, APHA, November 2002.
  - Egilman, D.S., Tobacco Marketing as an Anti-warnings Program, APHA, November 2002.
  - Egilman, D.S., Connolly, S., Golub, A., QAMA/McGill Corruption of the Epidemiologic Literature on Canadian Asbestos Mining, IEA World Conference of Epidemiology, August 2002.

- Egilman, D.S., Bagley, S., The Corporate Corruption of Epidemiology: The Asbestos, Beryllium, Tobacco Industries and the Role of Attorneys and Public Relations Firms, IEA World Conference of Epidemiology, August 2002.
- Egilman, D.S. Role of Insurance Companies in Industrial Health: Example of the Asbestos Tragedy, APHA, October 2001.
- Participant, Institute of Medicine, Division of Health Sciences Policy, Town Meeting on Clinical Research in the Public Interest, National Academy of Sciences, Washington, D.C. July 10-11, 1997.
- Kate Duran and Egilman, David: Corruption of IH Literature by Chemical Companies, APHA, Nov. 1991.
- Egilman, David, and Alexander Reinert: Corruption of the Asbestos Epidemiological Literature, APHA, Nov. 1991.
- Egilman, David: The Making of an Occupational/Environmental Disaster: The Corruption of the Asbestos Literature, Family Medicine Grand Rounds, Memorial Hospital of Rhode Island, Mar. 1991
- Egilman DS. Suppression Bias at the Journal of Occupational and Environmental Medicine. Int J Occup Environ Health 11(2):202-204, Apr-Jun 2005.
- Egilman DS and Bohme SR, Guest Editors. Over a Barrel: Corporate Corruption of Science and Its Effects on Workers and the Environment. Int J Occup Environ Health 11(4):331-337, Oct-Dec 2005.
- Egilman DS and Billings MA. Abuse of Epidemiology: Automobile Manufacturers Manufacture a Defense to Asbestos Liability. Int J Occup Environ Health 11(4):360-371, Oct-Dec 2005.
- Bohme SR, Zorabedian J, and Egilman DS. Maximizing Profit and Endangering Health: Corporate Strategies to Avoid Litigation and Regulation. Int J Occup Environ Health 11(4):338-348, Oct-Dec 2005.
- Egilman DS and Scout. Corporate Corruption of Science - The Case of Chromium (VI) (Commentary). Int J Occup Environ Health 12(2):169-176, Apr-Jun 2006.
- Egilman DS and Howe S. Against Anti-health Epidemiology: Corporate Obstruction of Public Health via Manipulation of Epidemiology. Int J Occup Environ Health 13(1):118-124, Jan-Mar 2007.
- Krumholz HM, Ross JS, Presler AH, and Egilman DS. What Have We Learnt from Vioxx? BMJ 334(7585):120-123, Jan 20, 2007.
- Egilman DS, Scout, Kol L, Hegg L, and Bohme SR. Manipulated Data in Shell's Benzene Historical Exposure Study (Commentary). Int J Occup Environ Health 13(2):222-232, Apr-May 2007.
- LaDou J, Teitelbaum DT, Egilman DS, Frank AL, Kramer SN, and Huff J. American College of Occupational and Environmental Medicine (ACOEM): A Professional Association in Service to Industry. Int J Occup Environ Health 13(4):404-426, Oct-Dec 2007.
- Ross JS, Hill KP, Egilman DS, and Krumholz HM. Guest Authorship and Ghostwriting in Publications Related to Rofecoxib: A Case Study of Industry Documents from Rofecoxib Litigation. JAMA 299(15):1800-1812, Apr 16, 2008.

- Hill KP, Ross JS, Egilman DS, and Krumholz HM. The ADVANTAGE Seeding Trial: A Review of Internal Documents. Ann Intern Med 149(4):251–-259, Aug 2008.
- Egilman DS and Bohme SR. IJOEH and the Critique of Bias (Editorial). Int J Occup Environ Health 14(2):147-151, Apr-Jun 2008.
- Krumholz SD, Egilman DS, and Ross JS. Study of Neurontin: Titrate to Effect, Profile of Safety (STEPS) Trial: A Narrative Account of a Gabapentin Seeding Trial. Arch Intern Med 171(12):1100-1107, Jun 27, 2011.
- Egilman DS and Druar NM. Corporate versus Public Interests: Community Responsibility to Defend Scientific Integrity. Int J Occup Environ Health 17(2):181-185, Apr-Jun 2011.
- Egilman DS, Ardolino EL, Howe S, and Bird T. Deconstructing a State-of-the-Art Review of the Asbestos Brake Industry. New Solut 21(4):545-571, 2011.
- Egilman DS, Bird T, and Lee C. MetLife and its Corporate Allies: Dust Diseases and the Manipulation of Science. Int J Occup Environ Health 19(4):287-303, Oct-Dec 2013.
- Egilman DS, Bird T, and Lee C. Dust Diseases and the Legacy of Corporate Manipulation of Science and Law. Int J Occup Environ Health 20(2):115-125, Apr-Jun 2014.
- Egilman DS and Monárrez R. Corporate Corruption of Science – Another Asbestos Example. Am J Ind Med 60(2):152-162, Feb 2017.
- Steffen JE, Fassler EA, Reardon KJ, Egilman DS. Grave Fraudulence in Medical Device Research: A Narrative Review of the PIN Seeding Study for the Pinnacle Hip System. Accountability in Research 25(1):37-66, Jan 2018. DOI 10.1080/08989621.2017.1405259
- Egilman, DS. The Production of Corporate Research to Manufacture Doubt About the Health Hazards of Products: An Overview of the Exponent Bakelite® Simulation Study. New Sol May 2018. http://dx.doi.org/10.1177/1048291118765485
- Egilman DS and Steffen JE. Commentary on "Assessment of Health Risk from Historical Use of Cosmetic Talcum Powder". (Accepted for publication: August, 2018.) DOI: http://dx.doi.org/10.1177/1048291118794166
- Bohme SR and Egilman DS. Beyond Reputation: Debate on the Role of Corporate Influence in Occupational and Environmental Medicine. New Solut 18(3):317-324, 2008.
- Egilman DS. Seeding Trials: Just Say No (Letter). BMJ 339:b4527 Nov 2, 2009.
- Egilman DS and Druar NM. Corporate versus Public Interests: Community Responsibility to Defend Scientific Integrity (Editorial). Int J Occup Environ Health 17(2):181-185, Apr-Jun 2011.
- Egilman DS and Bohme SR. Corporate Corruption of Science and its Effects on Workers and the Environment. Chain Reaction – The National Magazine of Friends of the Earth Australia 121:20-23, Jul 2014.
- Egilman DS and Tran T. A Commentary on Roggli's "The So-Called Short-Fiber Controversy". Int J Occup Environ Health DOI: 10.1080/10773525.2016.1153866, 2016.

- Egilman DS and Bohme SR. The suppression of science: How corporate interests hide the truth and how to stop them. Center for Science in the Public Interest Conference, Jul 2004.
- Egilman DS and Falender J. OxyContin: How Profits Took Priority over Public Health. APHA, Nov 2004.
- Egilman DS and Tran T. Manipulation in Data Presentation to the U.S. Food and Drug Administration (FDA) and the Public by DePuy Synthes. APHA, 2015.
- Fassler E, Steffen J, Egilman D. Corporate Manipulation of Law and its Impact on Chronic Disease. APHA 2018 Annual Meeting & Expo, San Diego, CA. Nov 10-14, 2018.

I have reached the conclusions stated below to a reasonable degree of medical probability based on my review of the medical and scientific literature, corporate documents, depositions and on my years of training and clinical experience.

3 METHODOLOGY

3.1 STATE OF THE ART MATERIALS REVIEWED

In the course of doing research, publishing peer-reviewed papers, corporate consulting in occupational and environmental health, and teaching courses, I base my opinions on the following sources of information:

- Review of medical literature:
  - Medical journal articles
  - Medical meetings
  - Medical textbooks
  - In order to review medical literature, I conducted computer searches of several different databases including:
    - Index Medicus
    - PubMed
    - NIOSHtic
    - EPA
    - Cancer Lit
    - MedLine
  - In addition, my staff or I reviewed each issue of Index Medicus from 1910 through 1966. (Index Medicus was computerized from 1964 forward and was reviewed by computer following this.)
- Review of published books
- Review of corporate documents
  - I have had access to the entire repository of documents and metadata has had been produced in this litigation. This repository includes production from the following sources:
    - ABCD – Amerisource Bergen
    - Allergan
    - Anda
    - Cardinal Health
    - CVS
    - DDM – Discount Drug Mart
    - Endo
    - HD Smith
    - Henry Schein
    - Insys
    - Janssen
    - Mallinckrodt
    - McKesson
    - Purdue
    - Rite Aid
    - Teva
    - Walgreens

        - Walmart
    - In addition to these, I reviewed legal complaints filed against opioid manufacturers and distributers in Massachusetts and Florida. When publicly available, I also reviewed the documents cited in these complaints.
    - I reviewed the Master Amended Complaint in this litigation.
    - My review of corporate documents included but was not limited to the following types of records:
        - Company meetings and correspondence
        - Internal company medical studies
        - Warnings labels and warnings policies
        - Promotional materials
        - Call notes
        - Marketing plans
        - CMEs
- Review of other produced documents
    - I reviewed documents from the Front Groups (organizations used by manufacturers to further promote their objectives)
    - I reviewed produced documents from Key Opinion Leaders
    - I reviewed produced documents from Advocacy Groups
    - I reviewed produced documents from Trade Groups
    - I reviewed produced documents from Professional Societies
- Review of depositions
    - Depositions (including exhibits) reviewed: I reviewed depositions taken in this case (Opiate MDL).

It is my expectation that I will review the Expert Reports of Plaintiffs' and Defendants' Experts once they are made available.

3.2 State of the Art Methods

I employed systematic search techniques in combination with a grounded theory approach. Grounded theory is an inductive method which allows analytical categories to emerge from the data presented.[1] A method of grounded theory analysis must build and change responsively throughout the research process. The grounded theory approach recognizes that data collection and analysis are inherently interrelated processes and calls for analysis to begin at the time of first data collection. The researcher, therefore, must continually ground their concepts and analyses in the reality of the data, which can protect against researcher bias. As described by Corbin and Strauss, "…the hypotheses are constantly revised during the course of the research until they hold true for the phenomena under study, as evidence in repeated interviews, observations, or documents."[2] This approach has

[1] Pope, Ziebland, and Mays 2000
[2] Corbin, J. and A. Strauss (1990). "Grounded Theory Research: Procedures, Canons and Evaluative Criteria." Zeitschrift fur Soziologie **19**(6): 418-427.

been used in analyses of corporate documents, which require the synthesis of a wide variety of information.[3] I have published a number of peer reviewed papers based on this method:

- Steffen JE, Fassler EA, Reardon KJ, Egilman DS. Grave fraudulence in medical device research: a narrative review of the PIN seeding study for the Pinnacle hip system. Accountability in Research 25(1):37-66, Jan 2018. DOI: 10.1080/08989621.2017.1405259
- Ross JS, Hill KP, Egilman DS. Guest authorship and ghostwriting in publications related to Rofecoxib: a case study of industry documents from rofecoxib litigation. JAMA 299(15):1800-1812, 2008. DOI: 10.1001/jama.299.15.1800
- Hill KP, Ross JS, Egilman DS, Krumholz HM. The ADVANTAGE seeding trial: a review of internal documents. Ann of Intern Med 149(4):251-258, 2008.
- Krumholz SD, Egilman DS, Ross JS. Study of Neurontin: titrate to effect, profile of safety (STEPS) trial. Arch Intern Med 171(12): 1100-1107.

I initially searched the sources above for key terms identified by me, including:

- Opioids
- Opioid addiction
- Pain
- NSAIDs
- Pseudo-addiction
- Pain treatment
- Analgesic
- Opioid efficacy
- Acupuncture
- Meditation
- Marijuana pain
- Homeopathy

After the emergent subset of documents was reviewed, key themes and concerns were identified, including documents specifically pertaining to evidence-based medicine, third party interest groups, public-private partnerships, EERW study design, chronic pain treatment, return-on-investment for marketing techniques, hospital licensing and accreditation, state medical board licensing, off-label promotion, diversion, and 12-hour dosing regimens. Additional searches were conducted to explore these and other more specific topic areas as they arose. This iterative analysis formed the basis for my state on the art opinions in this case.

[3] Steinman et al. 2006

3.3 EVIDENCE-BASED MEDICINE (EBM) METHODS

Evidence-based medicine (EBM) is an approach to medical decision-making meant to integrate "individual clinical expertise with the best available external clinical evidence from systematic research."[4,5] David Sackett described the importance of both external clinical evidence and individual clinical experience in providing effective medical care:[6]

> *Good doctors use both individual clinical expertise and the best available external evidence, and neither alone is enough. Without clinical expertise, practice risks becoming tyrannized by external evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient. Without current best external evidence, practice risks becoming rapidly out of date, to the detriment of patients.*

The practice of EBM can be outlined in five basic steps:[7,8]

1. Translation of uncertainty to an answerable question
2. Systematic retrieval of best evidence available
3. Critical appraisal of evidence for validity, clinical relevance, and applicability
4. Application of results in practice
5. Evaluation of performance

I implemented EBM in my medical practice beginning in the mid- to late-1980s following the publication of Dr. David Sackett's landmark book *Clinical Epidemiology*.[9] I also taught EBM to medical students as a Clinical Professor of Family Medicine at Brown University. Since its founding in 2002, I have headed GHETS (Global Health through Education, Training, and Service) and, through the organization, have implemented EBM curriculum in Asia, Africa, and Latin America.

3.3.1 Step 1: Translation of uncertainty to an answerable question

Answerable questions generally fall into two categories: "background" questions designed to examine the problem or disorder itself and "foreground" questions intended to address a specific problem, patient, or situation.[10] Background questions generally comprise of 1) a question root and verb and 2) some aspect of the disorder. Foreground questions usually

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[4] Sackett DL. Evidence-based medicine. *Semin Perinatol [Internet].* 1997 Feb 1 [cited 2019 Feb 28];21(1):3–5. Available from: https://www.sciencedirect.com/science/article/pii/S0146000597800134
[5] Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. BMJ. 1996;312(7023):71-2.
[6] Sackett DL. Evidence-based medicine. *Semin Perinatol [Internet].* 1997 Feb 1 [cited 2019 Feb 28];21(1):3–5. Available from: https://www.sciencedirect.com/science/article/pii/S0146000597800134
[7] Ibid.
[8] Dawes M, Summerskill W, Glasziou P, et al. Sicily statement on evidence-based practice. BMC Med Educ. 2005;5(1):1. Published 2005 Jan 5. doi:10.1186/1472-6920-5-1
[9] Sackett DL, Haynes RB, Tugwell P. Clinical epidemiology: a basic science for clinical medicine. 1st ed. Boston, MA: Little, Brown; 1985.
[10] Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. Evidence-Based Medicine: How to Practice and Teach EBM. 2nd Edition. Edinburgh, UK: Churchill Livingstone; 2000.

contain 1) the patient or problem of interest, 2) the main intervention, 3) comparison interventions, and 4) the desired clinical outcome.

I asked the following background questions:

- What are the treatment options for chronic non-cancer pain?

I asked the following foreground questions:

- In patients with chronic non-cancer pain, how do opioids and NSAIDs compare in terms of efficacy and adverse effects?

3.3.2 Step 2: Systematic retrieval of best evidence available

Once an answerable question has been posed, the researcher must select an evidence resource, execute a search strategy, and then evaluate the evidence summary.[11]

EBM tends to devalue textbooks as a source of best evidence because the information contained within them can quickly become out of date. For a textbook to be a dependable source of evidence, it should be revised frequently, be heavily referenced, and be comprised of evidence selected according to explicit principles of evidence.[12] Evidence databases, such as MEDLINE/PubMed, offer a better means for retrieving the best, most current evidence.[13]

In order to review medical evidence, I conducted computer searches of several different databases including:

- Index Medicus
- PubMed (MEDLINE)
- NIOSHtic
- EPA
- Cancer Lit
- MedLine

In addition to published evidence, I also searched corporate records for unpublished studies. I have had access to the entire repository of documents produced in this litigation. This repository includes production from the following sources:

- ABCD – Amerisource Bergen
- Allergan
- Anda
- Cardinal Health
- CVS
- DDM – Discount Drug Mart
- Endo
- HD Smith

[11] Ibid.
[12] Ibid.
[13] Ibid.

- Henry Schein
- Insys
- Janssen
- Mallinckrodt
- McKesson
- Purdue
- Rite Aid
- Teva
- Walgreens
- Walmart

I initially searched the sources above for key terms identified by me, including:

- Opioids
- Opioid addiction
- Pain
- NSAIDs
- Pseudo-addiction
- Pain treatment
- Analgesic
- Opioid efficacy
- Acupuncture
- Meditation
- Marijuana pain
- Homeopathy

Once these results were returned, I reviewed the abstracts, study description, or results (evidence summary) to determine whether each study generally addressed my questions.

3.3.3 Step 3: Critical appraisal of evidence for validity, clinical relevance, and applicability

First, the researcher must consider the type of study returned. Different guidelines may be used to critically appraise different types of studies. I used each of these, where appropriate, to inform my analysis.

3.3.3.1 Individual Studies

Questions for evaluating the results of an individual study:[14]

- Was the study randomized? Was the randomization concealed?
- Was follow-up sufficiently long and complete?
- Were all patients analyzed in the groups to which they were analyzed?
- Were patients and clinicians blinded to the treatment?
- Were groups treated equally apart from the experimental therapy?

[14] Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. Evidence-Based Medicine: How to Practice and Teach EBM. 2nd Edition. Edinburgh, UK: Churchill Livingstone; 2000.

- Were groups similar at the start of the trial?

Once an individual study has been evaluated and the results deemed valid, the importance of the results may be evaluated by asking two questions:[15]

- What is the magnitude of the treatment effect?
- How precise is the estimate of the treatment effect?

For qualitative differences in treatment efficacy between subgroups, it is advised these differences only be considered important when the answer to all four of the following questions is yes:[16]

- Does it make biological and clinical sense?
- Is the qualitative difference both clinically and statistically significant?
- Was the difference hypothesized before the study began (rather that the product of dredging the data) and has it been confirmed in other independent studies?
- Was it one of just a few subgroup analyses carried out in the study?

Finally, the EBM practitioner must ask whether the important results of a valid, individual study are applicable to the particular problem or patient at hand.

3.3.3.2 Systematic Reviews

Questions for evaluating the results of a systematic review:[17]

- Is this a systematic review of randomized trials?
- Does this systematic review have a "methods" section that describes:
    - Finding and including all relevant trials
    - How the validity of the individual studies was assessed?
- Were the results consistent from study to study?
- Were individual patient data in the analysis? Or was aggregate data used?

Once a systematic review has been evaluated and the results deemed valid, the importance of the results may be evaluated by asking two questions:[18]

- What is the magnitude of the treatment effect?
- How precise is the treatment effect?

Finally, the EBM practitioner must ask whether the important results of a valid systematic review are applicable to the particular problem or patient at hand.

3.3.3.3 Evidence of Harm

Questions for evaluating the validity of evidence of harm by a treatment:

[15] Ibid.
[16] Ibid.
[17] Ibid.
[18] Ibid.

- Were there clearly defined groups of patients, similar in all important ways other than exposure to the treatment (or other suspected cause)?
- Were treatments/exposures and clinical outcomes measured in the same ways in both groups? Was the assessment of outcomes either blinded to exposure or objectively measured?
- Was the follow-up of the study patients sufficiently long (for the outcome to occur and complete)?
- Do the results of the harm study fulfill some of the diagnostic considerations for causation?
    - Did exposure precede the outcome?
    - Is there a dose-response gradient?
    - Is there positive evidence from a "dechallenge-rechallenge" study?
    - Is the association consistent from study to study?
    - Does the association make biological sense?

Once the evidence of harm has been evaluated and deemed valid, the importance of the evidence may be evaluated by asking two questions:[19]

- What is the magnitude of the association between exposure and harm?
- How precise is the association between exposure and harm?

Finally, the EBM practitioner must ask whether the evidence of harm is applicable to the particular problem or patient at hand.

3.3.3.4 Guidelines for Levels of Evidence

Some EBM practitioners have created guidelines for categorizing and grading levels of evidence.

Canadian Task Force on the Periodic Health Examination's Levels of Evidence:[20]

II.2
III

[19] Ibid.

[20] Adapted from Canadian Task Force on the Periodic Health Examination. The periodic health examination. Can Med Assoc J 1979;121:1193-254

Levels of Evidence from Sackett:[21]

IV	His
V	Cas

Levels of Evidence for Therapeutic Studies:[22]

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5	

[21] Adapted from Sackett DL. Rules of evidence and clinical recommendations on the use of antithrombotic agents. Chest 1989;95:2S–4S

[22] From the Centre for Evidence-Based Medicine, http://www.cebm.net.

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence:[23]

* Level ma
studies, or

** As alwa

[23] OCEBM Levels of Evidence Working Group. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

As shown above, grading systems generally categorize systematic reviews of randomized control trials as the gold standard of evidence, followed by individual randomized control trials. The agencies which promulgate these grading systems often recognize that simplistic hierarchies ignore cases where observational studies, case-series, or even anecdotal evidence can provide definitive evidence and have made efforts to add greater nuance and flexibility to their grading scales.[24,25] GRADE guidelines also outline factors that may increase or decrease the strength of evidence from a particular study.[26,27] The GRADE factors which may decrease confidence in evidence are risk of bias, imprecision, inconsistency, indirectness, and publication bias. The GRADE factors which may increase confidence in evidence are large magnitude of effect, dose-response gradient, and cases where all plausible biases would decrease the magnitude of effect.[28]

Sackett (1997) cautioned against a "one-size-fits-all" approach to sources of evidence, but emphasized the important of randomized trials for assessing treatments:[29]

> *…in terms of study designs, evidence-based medicine is not restricted to randomized trials and meta-analyses. It involves tracking down the best external evidence with which to answer our clinical questions. To find out about the accuracy of a diagnostic test, its practitioners seek likelihood ratios, sensitivities, and specificities derived from proper cross-sectional studies of patients clinically suspected of harboring the relevant disorder, not a randomized trial. For a question about prognosis, they search for multivariate prediction rules generated from proper follow-up studies of patients assembled at a uniform, early point in the clinical course of their disease. Also, sometimes the evidence will come from the basic sciences such as genetics or immunology. **It is when asking questions about therapy that the practitioners of evidence-based medicine avoid the non-experimental approaches, because these routinely lead to false-positive conclusions about efficacy. Because the randomized trial, and especially the systematic review of several randomized trials, is so much more likely to inform clinicians and so much less likely to mislead them, it has become the "gold standard" for judging whether a treatment does more good than harm.*** [Emphasis added.]

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[24] OCEBM Levels of Evidence Working Group. "Background document: Explanation of the 2011 Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence." Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

[25] Guyatt GH, Oxman A, Vist G, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE an emerging consensus on rating quality of evidence and stren. Br Med J. 2008;336(7650):924–6.

[26] Ibid.

[27] https://bestpractice.bmj.com/info/us/toolkit/learn-ebm/what-is-grade/

[28] Guyatt GH, Oxman AD, Sultan S, Glasziou P, Akl EA, Alonso-Coello P, et al. GRADE guidelines: 9. Rating up the quality of evidence. Journal of clinical epidemiology. 2011;64(12):1311-6.

[29] Sackett DL. Evidence-based medicine. *Semin Perinatol [Internet].* 1997 Feb 1 [cited 2019 Feb 28];21(1):3–5. Available from: https://www.sciencedirect.com/science/article/pii/S0146000597800134

3.3.3.5 Evaluation of Funding Source and Conflicts of Interest

In addition to the factor reviewed above, funding source and conflicts of interest should be reviewed and considered for all studies. In their paper "How evidence-based medicine is failing due to biased trials and selective publication," EBM practitioners Every-Palmer and Howick reached the following conclusions about the effect of industry funding on EBM practice:[30]

> *We argue EBM's indiscriminate acceptance of industry-generated 'evidence' is akin to letting politicians count their own votes. Given that most intervention studies are industry funded, this is a serious problem for the overall evidence base. Clinical decisions based on such evidence are likely to be misinformed, with patients given less effective, harmful or more expensive treatments.*

The authors also provide a list of examples of methods for pharmaceutical companies to get the results they want from clinical trials:[31,32]

- Conduct a trial of your drug against a treatment known to be inferior.
- Trial your drugs against too low a dose of a competitor drug.
- Conduct a trial of your drug against too high a dose of a competitor drug (making your drug seem less toxic).
- Conduct trials that are too small to show differences from competitor drugs.
- Use multiple end points in the trial and select for publication those that give favorable results.
- Do multicenter trials and select for publication results from centers that are favorable.
- Conduct subgroup analyses and select for publication those that are favorable.
- Present results that are most likely to impress – for example, reduction in relative rather than absolute risk.

Every-Palmer and Howick recommend adopting industry bias as a factor in guidelines for evaluating levels of evidence:[33]

> *Evidence-ranking schemes need to be modified to take the evidence about industry bias into account. There are already mechanisms within EBM evidence-ranking schemes to up- or downgrade evidence based on risk of bias. For example, the Grading of Recommendation Assessment, Development and Evaluation (GRADE) system allows for upgrading observational evidence demonstrating large effects, and downgrading randomized trials for failing to adequately conceal allocation (and various other factors) [65]. However,*

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[30] Every-Palmer S, Howick J. How evidence-based medicine is failing due to biased trials and selective publication. J Eval Clin Pract. 2014;20(6):908–14.
[31] Ibid.
[32] Smith, R. (2005) Medical journals are an extension of the marketing arm of pharmaceutical companies. PLoS Medicine, 2 (5), e138.
[33] Every-Palmer S, Howick J. How evidence-based medicine is failing due to biased trials and selective publication. J Eval Clin Pract. 2014;20(6):908–14.

> *currently such schemes are agnostic to the origins of evidence and do not expressly recognize the high risk of bias when the producers of evidence have an invested interest in the results**. It would be easy to introduce an evidence quality item based on whether a trial was conducted or funded by a body with a conflict of interest. If so, the evidence could be downgraded. Given the failure of current evidence-ranking schemes to detect and rule out industry-funding bias, this is a necessary step if EBM critical appraisal is to remain credible.***
> [Emphasis added.]

For these reasons, I included funding source and industry bias as one of the factors which would decrease my confidence in a particular source of evidence.

3.3.4 Step 4: Application of results in practice

This step speaks for itself. Once a critical analysis of the evidence has been completed, the findings can be applied to the situation at hand.

In this case, I applied my results in the form of my expert opinions.

3.3.5 Step 5: Evaluation of performance

Guidelines exist for self-evaluation of each of the previous steps of EBM practice.[34]

Self-evaluation for asking answerable questions:

- Am I asking any clinical questions at all?
- Am I asking well-formulated questions (based on the guidelines reviewed above)?
- Am I using a "map" to locate my knowledge gaps and articulate questions?
- Can I get myself "unstuck" when asking questions?
- Do I have a working method to save my questions for later answering?
- Am I modeling the asking of answerable questions for my learners?
- Am I writing any educational prescriptions in my teaching? Are they being "filled"?
- Are we incorporating question asking and answering into everyday activities?
- How well am I guiding my learners in their question asking?
- Are my learners writing educational prescriptions for me?

Not all of these questions applied to my practice of EBM in this context. Of those which did apply, I found that my performance was satisfactory.

Self-evaluation for finding the best external evidence:

- Am I searching at all?
- Do I know the best sources of current evidence for my clinical discipline?
- Have I achieved immediate access to searching hardware, software, and the best evidence for my clinical discipline?
- Am I finding useful external evidence from a widening array of sources?

[34] Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. Evidence-Based Medicine: How to Practice and Teach EBM. 2nd Edition. Edinburgh, UK: Churchill Livingstone; 2000.

- Am I becoming more efficient in my searching?
- Am I using MeSH headings, thesaurus, limiters, and intelligent free text when searching MEDLINE?
- How do my searches compare with those of research librarians or other respected colleagues who have a passion for providing best current patient care?

I found that my performance was satisfactory.

Self-evaluation for critically appraising the evidence for its validity and potential usefulness:

- Am I critically appraising external evidence at all?
- Are the critical appraisal guides becoming easier for me to apply?
- Am I becoming more accurate and efficient in applying some of the critical appraisal measures?
- Am I creating any CATS (critically appraised topics)?

Not all of these questions applied to my practice of EBM in this context. Of those which did apply, I found that my performance was satisfactory.

Self-evaluation for applying results in practice:

- Am I integrating my critical appraisals into my practice at all?
- Am I becoming more accurate and efficient in adjusting some of the critical appraisal measures to fit my individual patients?
- Can I explain and resolve disagreements about management decisions in terms of this integration?
- Have I conducted any clinical decision analyses?
- Have I carried out any audits of my diagnostic, therapeutic, or other EBM performance?

Not all of these questions applied to my practice of EBM in this context. Of those which did apply, I found that my performance was satisfactory.

4 DEFINITIONS

4.1 CHRONIC PAIN

As referred to herein, "chronic pain" is pain that has persisted after reasonable medical efforts have been made to relieve the pain or cure its cause and that has continued, either continuously or episodically, for longer than three continuous months.

See **Exhibit B.16.**

4.2 ADDICTION

As referred to herein, "addiction" is a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance use and includes: a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal.

See **Exhibit B.367.**

4.3 TOLERANCE

As referred to herein, "tolerance" is the condition of a patient receiving, for one week or longer, at least 60 mg oral morphine/day, 25 mcg transdermal fentanyl/hour, 30 mg oral oxycodone/day, 8 mg oral hydromorphone/day, 25 mg oral oxymorphone/day, or an equianalgesic dose of another opioid.

See **Exhibit B.15.**

4.4 THE "VENTURE"

As referred to herein, the "Venture" refers to all Defendants in the Opiate Litigation (including their associated individuals and/or organizations) acting in a concerted fashion separately or together to effect a particular objective.

See **Exhibit B.473.**

4.5 ADDITIONAL DEFINITIONS

I use a number of industry specific terms. These are more fully defined in **Exhibit B.401**.

5 CAPSULE OF OPINIONS

The "Venture" acted in concert to:

1. Undermine the risks of opioid addiction;
2. Expand the market for opioid use by:
    a. Expanding the indications for use;
    b. Increasing the amount of opioids approved for use; and
    c. Manipulating the doctors' perceptions of the relative risks, benefits and potency of opioids.
    d. Capitalizing on doctor's misperceptions of the relative risks, benefits and potency of opioids.
    e. Recommending that opioids be used for chronic non-malignant pain.
    f. Defining pain as a disease, and not a symptom;
3. Target inappropriate prescribers, including:
    a. Those prescribers who were not knowledgeable in the use of potent opioids for the management of chronic non-malignant pain.
    b. Those prescribers who were likely sources of abuse and diversion;
4. Circumvent prescribing physicians by marketing directly to consumers as well as health care professionals, formularies, medical and nursing schools and state medical boards to promote increased use of opioids;
5. Overstate the efficacy and appropriateness of opioid analgesics in the treatment of chronic non-malignant pain and fail to warn of the risk of hyperalgesia;
6. Create and establish the myths around dosing, including but not limited to,
    a. Dose frequency is fixed;
    b. Titration should only be upward;
    c. There is no ceiling dose;
    d. The half-life elimination is the same for every human being on Earth;
7. Strategically utilize third parties, including but not limited, to front groups, key opinion leaders, advocacy groups, unbranded promotion, professional societies, trade groups, company-sponsored non-drug specific promotion, and continuing education programs, to create the conditions necessary.

See below, **Point 6**, and **Exhibits** hereto attached, including **Exhibits B.7, B.18, B.68, B.337, B.369, and B.404.**

6 IN 2004, I WARNED ABOUT THE CRISIS; I WAS IGNORED

In 2004, I told Purdue Pharma the following facts and opinions. I hold the same opinions today. Purdue ignored this documented misconduct and continued to mislead the medical community about the addiction potential of their opioid drugs and expanded the market to encourage use in patients for whom the drugs' risks exceeded their benefits. In addition, after I described these problems to them, Purdue marketed a new opioid, Palladone, whose risks outweighed its benefits. https://www.fda.gov/Drugs/DrugSafety/ucm129288.htm

1. OxyContin is a Schedule II narcotic which was approved by the Food and Drug Administration in 1995. The main ingredient in OxyContin is oxycodone, which is a synthetic, morphine-like substance. **The drug was originally marketed for the management of moderate to severe pain where use of an opioid analgesic is appropriate for more than a few days, like cancer pain.** However, Purdue Pharma has aggressively marketed OxyContin through an advertising campaign that misled health providers and the public about the dangers of OxyContin. In many ways, Purdue's marketing strategy was formulated to assuage the disquiet of patients and physicians regarding the risks of abuse, diversion, addiction and death by overdose of OxyContin. Purdue Pharma developed the marketing piece "Myths about Opioids" to overcome the obstacle of physicians fearing that putting their patients on an opioid like OxyContin could cause them to become addicted. One of Purdue's "myths" was "Opioid addiction (psychological dependence) is an important clinical problem in patients with moderate to severe pain treated with opioids."[35] In actuality, the myth wasn't the risk of addiction, but the evidence they used to dispel this "myth."

2. As a practicing physician who had an active primary care practice, Purdue's information on OxyContin, as provided in the *Physicians Desk Reference* gave me the impression that in general, patients would not become addicted to OxyContin if it were prescribed to them for pain. Unfortunately, I first became aware of the serious problems associated with OxyContin use through experiences with my patients which contradicted the promising scenario Purdue provided in its marketing materials and "warnings." My patient experience revealed that addiction was a serious consequence of the prescription of OxyContin for pain.

3. A review of the product labeling for OxyContin from 1999 to 2001 underscores Purdue's failure to warn adequately regarding abuse or addiction. Some of the major inadequacies

[35] "Dispelling Myths about Opioids," Purdue Pharma.

of the labels comprise omissions of pertinent information and misrepresentations about the characteristics of OxyContin. I provide some examples below.

The omissions include:

a. Purdue failed to include "prior drug addiction" under the "Contraindications section" for the use of OxyContin. Instead, under a different section called "Use in Drug Abuse and Addiction" the statement was limited to "[OxyContin] has no approved use for the management of addictive disorders,"[36,37,38]

b. Purdue failed to include the risk of addiction in the label's "Warning" or "Precautions" sections;[39]

c. Purdue omitted from the "Information for Patients/Caregivers" a warning that repeated administration could lead to addiction;[40]

d. Purdue failed to list any of the symptoms of opioid withdrawal;[41]

The misrepresentations include:

e. Purdue told physicians that "delayed absorption, as provided by OxyContin tablets, is believed to reduce the abuse liability of a drug."[42] This is unsupported by any study and in fact while it is true that OxyContin has a slower release component, OxyContin also has a fast release component. "OxyContin Tablets exhibit a biphasic absorption pattern with two apparent absorption half times of 0.6 and 6.9 hours, which describes the initial release of oxycodone from the tablet followed by a prolonged release."[43] Therefore, if delayed release reduced the likelihood of addiction then this drug would increase the risk of addiction.

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[36] *Physicians' Desk Reference*, OxyContin Package Insert, 53rd ed. Montvale, NJ: Thompson PDR. 1999: 2572.
[37] *Physicians' Desk Reference*, OxyContin Package Insert, 54th ed. Montvale, NJ: Thompson PDR, 2000:2539.
[38] *Physicians' Desk Reference*, OxyContin Package Insert, 55th ed. Montvale, NJ: Thompson PDR, 2001.
[39] *Physicians' Desk Reference*, OxyContin Package Insert, 1999, 2000 and 2001.
[40] Ibid.
[41] Ibid.
[42] Ibid.
[43] *Physicians' Desk Reference*, OxyContin Package Insert, 57th ed. Montvale, NJ: Thompson PDR, 2003, 2852.

f. Purdue stated that "tolerance and physical dependence in pain patients are not signs of psychological dependence."[44] This is not true. Tolerance and physical dependence to a drug are typical, hallmark, diagnostic symptoms of substance dependence. *The Diagnostic and Statistical Manual of Mental Disorders* describes the criteria for substance dependence which include both tolerance and withdrawal. "Criteria for Substance dependence: (1) Tolerance, as defined by either of the following: (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect (b) markedly diminished effect with continued use of the same amount of the substance. (2) withdrawal, as manifested by either of the following: (a) the characteristic withdrawal syndrome for the substance (b) the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms."[45]

4. The inadequacy of the OxyContin warning label is further underscored when it is compared to other addictive oral, controlled-release opioid analgesics containing morphine sulfate, MS Contin (Purdue Frederick) and OraMorph SR (Roxane). Both of these are marketed as controlled-release 12-hour pain control products like OxyContin and are Schedule II drugs with the same abuse liability as OxyContin. However, their labels are strikingly different, even though Purdue authored both the MS Contin and OxyContin labels.

5. Unlike the OxyContin label, the labels for MS Contin and OraMorph SR state that the product may cause addiction upon repeated use. The MS Contin label states that "psychological and physical dependence may develop upon repeated administration."[46] The OxyContin label does not address issues related to psychological and physical dependence. The OraMorph SR (Roxane) label acknowledges the addiction risk even more clearly: "Morphine is the most commonly cited prototype for a narcotic substance that possesses an addiction-forming or addiction-sustaining liability. A patient may be at risk for developing dependence to morphine if used improperly or for overly long periods of time."[47] Unlike the OraMorph label, OxyContin fails to alert physicians that, "Individuals with a history of opioid or other substance abuse or dependence, being more apt to respond to euphorogenic and reinforcing properties of morphine, would be considered to be at greater risk."

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[44] *Physicians' Desk Reference*, OxyContin Package Insert, 1999, 2000 and 2001.
[45] *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Washington, D.C.: The American Psychiatric Association, 1994: 181.
[46] *Physicians' Desk Reference*, MS Contin Package Insert, 57th ed. Montvale, NJ: Thompson PDR, 2003, 2835.
[47] *Physicians' Desk Reference*, OraMorph Package Insert, 56th ed. Montvale, NJ: Thompson PDR, 2002, 3063.

6. Also, unlike the OxyContin label, the OraMorph SR label does not emasculate statements regarding addictive potential by citing the product's "delayed absorption" characteristics. Unlike the OxyContin label, the OraMorph SR label does not minimize addiction concerns by proclaiming that "reports" of addiction are "rare." Purdue claimed that reports of addiction were rare before the drug was marketed; however, Purdue never performed any tests for addiction in its pre-market trials and health care providers could not make "reports" before Purdue sold the drug. In fact, soon after Purdue marketed the drug reports of addiction became all too common. They were so common in fact, that local newspapers began to report this problem in 1999. A search of LexisNexis revealed hundreds of press reports by 2001. There were not a comparable number of press reports for either MS Contin or OraMorph SR. In comparison to OxyContin, reports of addiction from other comparable drugs were "rare."

7. See attached table for further comparisons between the OxyContin, MS Contin and Percocet package inserts. (for table, see **Exhibit B.455**)

8. Purdue Pharma's own internal reports highlight problems with prescription drug abuse back to 2001. In 2001, a Purdue newsletter called "@purdue" included an article entitled, "A Busy Schedule for Dr. Haddox Produces Some Balanced Media." (See attached as Exhibit 1.) The article describes how Purdue has sent one of their most prominent physicians, Dr. Haddox, to the Appalachian States, "visiting the communities most affected by the abuse and diversion of OxyContin Tablets." Purdue reported that over a seven-month period, Dr. Haddox was on the road for 122 days dealing with "reports" and abuse of OxyContin. As a practicing physician, I would have wanted to know that one of Purdue's head doctors was traveling for 122 days dealing with issues of drug addiction related to OxyContin use. This would have allowed me to gauge the extent of the problem and would have allowed me to place the "rare reports" of addiction statement in perspective.

9. Beginning with the launch of the drug in 1996 Purdue's OxyContin physician-directed promotional pieces, including advertisements, brochures, and videos, asserted that, "less than 1% of patients taking opioids actually become addicted."[48] They also asserted that the development of addiction to opioid medication is "rare," and classify as "myth" that "opioid addiction (psychological dependence) is an important clinical problem in patients

[48] "Dispelling Myths about Opioids," Purdue Pharma.

with moderate to severe pain treated with opioids."[49,50] These statements are wrong and/or unsupported by any scientific evidence.

10. Purdue Pharma supports and maintains a website which discusses pain and promotes its product. Unfortunately, it also uses this site to misinform health care providers and patients about the risks of use of OxyContin. The website is called, "Partners Against Pain," and includes articles such as "A Guide to Your New Pain Medication and How to Become a Partner Against Pain."[51] This article followed the "Frequently Asked Questions" format and asked, "Aren't opioid pain medications like OxyContin Tablets "addicting"? Even my family is concerned about this." Purdue proffered the following mischaracterization of addiction: "Drug addiction means using a drug to get "high" rather than to relieve pain. You are taking opioid pain medication for medical purposes. The medical purposes are clear and the effects are beneficial, not harmful. True addiction rarely occurs when opioids are being used properly under medical supervision to relieve pain." The "guide to patients" misleads patients into believing that their motivation for taking OxyContin (i.e., for pain instead of to "get high") is the sole determinant of whether they are, or will become, addicted to their pain medication.

11. In 2001, in another question and answer section of the website, under the heading "Patient/Caregiver", Partners against Pain declared: "When you feel pain, your pain is real… Remember: You have every right to ask [doctors and nurses] to help you relieve the pain as much as possible." This answer is self-serving and scientifically flawed. Medical literature notes that addiction pain and physiological pain overlap, and separating them presents unique challenges to the physician.[52] Addiction has been shown to make patients even more sensitive to pain - and thus more likely to request pain medications.[53] For example hyperalgesia, or diminished pain tolerance, is a sign of opioid withdrawal.[54] Patients who are dependent on opioid medication will sometimes undergo withdrawal symptoms that manifest as pain.[55] Implying that patients have a right to as much opioid as they wish minimizes the risk of addiction and perpetuates misinformation about addiction and pain perception.

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[49] Ibid.
[50] "I Got My Life Back," Partners Against Pain Brochure, Purdue Pharma, 1997, 8700300165.
[51] Partners Against Pain website, Available at: http://www.partnersagainstpain.com/html/main/index.htm, Acessed on September 8, 2003.
[52] Compton, P., and Gebhart, G.F., "The Neurophysiology of Pain in Addiction," as seen in The Principles of Addiction Medicine, American Society of Addiction Medicine, (2nd ed. 1998), at 901, 912-914.
[53] Ibid. at 912.
[54] Ibid.
[55] Dickinson, "Use of Opioids to Treat Chronic, Noncancer Pain," *West J Med* 2000; 172:107, 111.

12. Purdue has also misled patients through their production of a pamphlet and informational video, "From One Pain Patient to Another," which encouraged patients to doctor-shop to find providers who were most willing to prescribe narcotics. Purdue told patients, "Don't be afraid about the things you've heard about these drugs [opioids]," and, "...find the right doctor"… "I think it is very unfortunate that so many physicians are reluctant to treat people like me, who have moderate chronic pain, with opioids." Purdue thus disparaged the conservative and cautious prescribing practices of many responsible health practitioners. Again, Purdue actively misinformed and inadequately warned patients and physicians of the addiction risks and withdrawal symptoms associated with OxyContin.

13. Purdue has centered its promotional and marketing focus for OxyContin on the twice a day, every 12-hour dosing schedule. For example, when OxyContin was first introduced, Purdue stated that OxyContin offered a "significant advantage" because "unlike short-acting pain medications, which must be taken every 3 to 6 hours—often on an "as needed basis," OxyContin tablets are taken every 12 hours, providing smooth and sustained pain control all day and all night." Purdue's 1998 OxyContin Budget Plan describes the importance of q12 dosing to sales, "Our marketing research indicates that the most important feature of OxyContin tablets, beyond the familiarity of oxycodone, is the q12h dosing schedule. In all seven pre-launch market research projects conducted among 626 healthcare professionals, this was the most compelling reason to prescribe the OxyContin Tablets."[56]

14. However, Purdue's marketing materials did not tell the entire story about the effective dose interval. In most clinical studies, OxyContin pain relief did not last for 12 hours. One of the first clinical trials showed that "half of the patients used IR (immediate release) oxycodone rescue almost daily," revealing that the drug was not able to relieve pain for the full 12-hour dosing schedule.[57] Scientists at Purdue and other independent labs conducted a number of clinical tests that found that OxyContin did not relieve pain for 12 hours. (Hagen and Babul, 1997, Kaplan et al, 1998) Hagen and Babul showed that a significant percentage of patients on OxyContin and Hydromorph Contin required rescue analgesic. They reported that, "the percentage of rescue analgesic use in the first, second and third 4-hour periods representing the combined 12-hour dosing frequency of controlled release oxycodone… was 23.8%, 42.8% and 33.3% for controlled release oxycodone (OxyContin.)"[58] Kaplan et al similarly found that, "Among patients enrolled, after the amendment that allowed titration and rescue, 18 of 29 (62%) who received CR

[56] Purdue Pharma Budget Plan, 1998, 4-41.
[57] Citron ML, Kaplan R, Parris WC et al, Long-Term Administration of Controlled-Release Oxycodone Tablets for the Treatment of Cancer Pain, *Cancer Investigation*, 1998;16(8): 563.
[58] Hagen NA, Babul N, Comparative Clinical Efficacy and Safety of a Novel Controlled-Release Oxycodone Formulation and Controlled-Release Hydromorphone in the Treatment of Cancer Pain, *Cancer*, 1997 Apr 1;79(7): 1432.

oxycodone needed at least one supplemental (rescue) dose… During the day, the median time to first rescue use was 4 hours for the CR (OxyContin) group."[59]

Below is a summary of my opinions followed by a compilation of materials that I read reviewed or considered in compiling these opinions:

1) Purdue Pharma's marketing was inappropriate and led to the abuse and misuse of OxyContin.
   a) Purdue Pharma marketed OxyContin based on claims that were scientifically invalid or unproven. For example:
      i) Purdue stated that "less than 1% of patients taking opioids actually become addicted" without any clinical data or valid scientific references.
         (1) Purdue misinformed their sales representatives for OxyContin. When asked in a quiz during one of the sales representatives training sessions a question concerning the risk of iatrogenic addiction, Purdue told them the correct answer was "less than one percent."
      ii) Purdue said that iatrogenic addiction did not occur. Instead, they suggested that addiction only occurred when OxyContin was taken for illicit use. This is not true.
         (1) William Gergely, a former Purdue district sales manager, told the Florida Attorney General that top sales officials had described OxyContin as "non-habit forming." Sales representatives were taught to tell doctors that drug abusers would not be interested in OxyContin.
   b) Purdue failed to include adequate warnings about the risk of addiction in their marketing materials. For example:
      i) Purdue was cited by the FDA on numerous occasions for failing to include adequate warnings on advertisements. The FDA cited Purdue in May of 2000 for an advertisement stating that OxyContin can be used for arthritis pain when in actuality; OxyContin is not a first-line therapy for arthritis. Purdue was later cited in 2002 for two advertisements in the Journal of the American Medical Association that failed to describe and adequately present the possible risks of taking OxyContin.
   c) OxyContin was recommended for inappropriate uses in marketing materials.
      i) OxyContin was promoted for osteoarthritis sufferers and "weekend warriors" as a substitute for much weaker and safer pain medications.

[59] Kaplan R, Parris WC, Citron ML, et al, Comparison of Controlled-Release and Immediate-Release Oxycodone Tablets in Patients with Cancer Pain. J Clin Oncol. 1998 Oct;16(10):3232-33.

ii) Purdue manipulated the FDA approval process to assist in their marketing of OxyContin for treatment of osteoarthritis.

d) Purdue inappropriately marketed OxyContin for q12h dosing.

2) Purdue Pharma's warnings for Oxycontin were inappropriate and led to the abuse and misuse of OxyContin.

a) Purdue's Product labeling for OxyContin fails to warn adequately regarding abuse or addiction.

i) Unlike similar drugs, OxyContin's patient package insert does not state that the product may cause addiction nor does it directly acknowledge the risk of narcotic dependence.

ii) Purdue Pharma's warning labels in Europe have much stronger warnings about addiction risk than their warning for United States patients.

b) Purdue used an FDA reprimand to expand the indications of OxyContin.

3) Purdue Pharma's information about dose and drug kinetics was wrong.

a) Purdue Pharma had no data to support their patent claims that at a dose range of 10 to 40 every 12 hours, pain would be controlled in 90% of patients.

b) Purdue told physicians to prescribe OxyContin for q12 h dosing while Purdue had information that proved that most patients needed to be dosed at different intervals.

c) Purdue's dosing recommendation for Oxy IR drugs was based on marketing and other considerations, but not science. Purdue either recommended too frequent use of Oxy IR (q6) or used inadequate doses of IR in its OxyContin efficacy trials (q6 vs q4-6) or both.

d) Purdue has inaccurately made claims that "delayed absorption is believed to reduce the abuse liability of a drug." Purdue has no scientific evidence to prove this claim nor have they ever tested the merits of this claim.

e) Fundamental pharmacokinetic principles establish that, for a fixed total daily dose of OxyContin, peak plasma concentrations of oxycodone will be slightly lower, troughs in plasma concentrations of oxycodone will be slightly higher, and overall fluctuation in plasma concentrations will be slightly less, if OxyContin is administered every 8 hours than if OxyContin is administered every 12 hours. Purdue emphasized 12 hour dosing because the 12 hour dosing schedule represented a significant competitive advantage of OxyContin over other products.

4) Purdue failed to institute post market surveillance. They failed to use the IMS system to determine the location of "pill mills" or problem physicians. They failed to establish a monitoring system for addiction issues and failed to monitor emergency rooms for deaths and other serious side effects associated with drug use. They may have monitored internet chat rooms but failed to compile or organize this information.

5) Purdue greatly expanded the problem of drug addiction and caused or contributed to numerous deaths.

7 ADDITIONAL OPINIONS SINCE 2004

7.1 OPINION – 2004-7 INVESTIGATIONS INCLUDES OFF LABEL USES AND BAD REP BEHAVIOR FOR CEPHALON (TEVA)

See **Exhibit B.1** hereto attached.

7.2 OPINION – IN 2011, WALGREENS PHARMACISTS WERE OPENING SECOND PHARMACIES UNDER FAMILY MEMBERS' NAMES - UNDER PRESSURE TO FILL SCRIPTS NOT CONTROL THEM.

See **Exhibit B.2** hereto attached.

7.3 OPINION – WALGREENS SYSTEMS COULD BE MANIPULATED TO ALLOW STORES TO CIRCUMVENT QUANTITY RESTRICTIONS - KNOWN ISSUE - 'THIS IS HOW THE SYSTEM ALWAYS WORKED'.

See **Exhibit B.3** hereto attached.

7.4 OPINION – THE "VENTURE" BRIBED THE SAME DOCTORS TO OVERPRESCRIBE.

See **Exhibit B.4** hereto attached.

7.5 OPINION – THIS IS A DESCRIPTION OF DRUG PAYMENT FLOWS. I AGREE.

See **Exhibit B.5** hereto attached.

7.6 OPINION – ACTAVIS PRESCRIPTION COUPONS DO NOT WARN OF ADDICTION RISKS AND OFFER $1200 OFF PER YEAR.

See **Exhibit B.6** hereto attached.

7.7 OPINION – THE "VENTURE" ACTED IN CONCERT TO UNDERMINE THE RISKS OF OPIOID ADDICTION.

See **Exhibit B.7** hereto attached.

7.8 ALL FOR ONE AND ONE FOR ALL – THE "VENTURE" KNEW COLLECTIVE MARKETING INCREASED THE SIZE OF THE OPIOID PIE. SIMILARLY HAD ANY "VENTURE" MEMBER BROKEN RANKS, THE OPIOID MARKET WOULD HAVE SLOWED OR IF THE COMPLETE TRUTH WAS TOLD (NO EFFICACY AND HIGH ADDICTION RISK) THE MARKET WOULD HAVE CRASHED.

See **Exhibit B.8** hereto attached.

7.9 OPINION – THERE IS NO SCIENTIFICALLY AUTHORITATIVE EVIDENCE TO SUPPORT THE CLAIM THAT OPIOIDS ARE MORE EFFECTIVE THAN PLACEBO AND OTHER NON-OPIOID ALTERNATIVES FOR CHRONIC NON-MALIGNANT PAIN. THERE IS EVIDENCE THAT OPIOIDS ARE NO MORE EFFECTIVE THAN NON-OPIOID ALTERNATIVES FOR CHRONIC NON-MALIGNANT PAIN.

See **Exhibit B.9** hereto attached.

7.10 OPINION – I AGREE WITH ASHP (AMERICAN SOCIETY OF HOSPITAL PHARMACISTS) FORMULARY MANAGEMENT GUIDELINE

See **Exhibit B.10** hereto attached.

7.11 OPINION – PATIENTS TREATED WITH PRESCRIPTION OPIOIDS GET ADDICTED.

See **Exhibit B.11** hereto attached.

7.12 OPINION – CARDINAL FAILED TO TAKE ACTION FOR SUSPICIOUS ORDERS.

See **Exhibit B.12** hereto attached.

7.13 OPINION – COLLABORATION AND PEER INFLUENCE YIELD FORMULARY ACCESS FOR JANSSEN IN CLEVELAND

See **Exhibit B.13** hereto attached.

7.14 OPINION – COMPANIES SHOULD NOT MARKET NARCOTICS TO ELEMENTARY SCHOOL STUDENTS DIRECTLY OR INDIRECTLY.

See **Exhibit B.14** hereto attached.

7.15 OPINION – OPIOID TOLERANCE IS DEFINED AS:

See **Exhibit B.15** hereto attached.

7.16 OPINION – THE OHIO DEFINITION OF CHRONIC PAIN.

See **Exhibit B.16** hereto attached.

7.17 OPINION – DICTIONARY OF TERMS FOR WHOLESALER AGREEMENTS

See **Exhibit B.17** hereto attached.

7.18 OPINION – THE "VENTURE" ACTED IN CONCERT TO CIRCUMVENT PRESCRIBING PHYSICIANS BY MARKETING DIRECTLY TO CONSUMERS AS WELL AS HEALTH CARE PROFESSIONALS, FORMULARIES, MEDICAL AND NURSING SCHOOLS AND STATE MEDICAL BOARDS TO PROMOTE INCREASED USE OF OPIOIDS.

See **Exhibit B.18** hereto attached.

7.19 OPINION – DISCONTINUATION OF OPIOIDS REDUCES PAIN IN SOME PATIENTS

See **Exhibit B.19** hereto attached.

7.20 OPINION – DISTRIBUTORS DISPENSE IN DOCTORS' OFFICES AND CLINICS AND OFFER PRACTICE MANAGEMENT TOOLS.

See **Exhibit B.20** hereto attached.

7.21 OPINION – WALGREENS SOLUTION TO RED FLAGGED STORES WAS TO FIND A DISTRIBUTER WHO WOULD SELL TO THEM. ALL 3 WALGREENS DISTRIBUTOR FACILITIES FAILED TO IMPLEMENT SOM PROCEDURES.

See **Exhibit B.21** hereto attached.

7.22 OPINION – THE "VENTURE" EXPANDED THE MARKET BY PROMOTING INAPPROPRIATE USE (LOW BACK SPASM) OF 3 YEARS DURATION WITH "SOME PAIN".

See **Exhibit B.22** hereto attached.

7.23 OPINION – THE "VENTURE" INTRODUCED THE CONCEPT OF THE "5TH VITAL SIGN" IN 1995, BUT LATER ALLOWED AMERICAN PAIN SOCIETY TO PROMOTE IT AS ITS OWN CREATION TO ENHANCE THE SALES OF OPIOIDS.

See **Exhibit B.23** hereto attached.

7.24 OPINION – ABBOTT AND PURDUE TARGETED INAPPROPRIATE PHYSICIANS FOR USE OF OPIOIDS FOR CHRONIC PAIN.

See **Exhibit B.24** hereto attached.

7.25 OPINION – AMERICAN PAIN FOUNDATION ("APF") FRONTED FOR INDUSTRY TO INCREASE SALES.

See **Exhibit B.25** hereto attached.

7.26 OPINION – "VENTURE" MEMBER ENDO FUNDED SEVERAL FRONT ORGANIZATIONS AND FUNDED NIH PUBLICATIONS AND VARIOUS "EDUCATIONAL" EVENTS.

See **Exhibit B.26** hereto attached.

7.27 OPINION –CEPHALON'S ACTIQ WAS NOT INDICATED FOR, BUT WAS MARKETED OFF LABEL FOR MINOR PAIN.

See **Exhibit B.27** hereto attached.

7.28 OPINION – CHRONIC LONG ACTING OPIOIDS ARE NOT INDICATED FOR TREATMENT OF OSTEOARTHRITIS, LOW BACK PAIN OR FIBROMYALGIA. OPIOIDS ARE NOT INDICATED AT ALL FOR RHEUMATOID ARTHRITIS OR FIBROMYALGIA.

See **Exhibit B.28** hereto attached.

7.29 OPINION – CORPORATE INTEGRITY AGREEMENTS INDICATING THAT EACH OF THESE COMPANIES VIOLATED FDA RULES.

See **Exhibit B.29** hereto attached.

7.30 OPINION – DOCTORS ON THE "VENTURE'S" PAYROLL ADMITTED THAT PSEUDOADDICTION DESCRIBES BEHAVIORS 'CLEARLY CHARACTERIZED AS DRUG ABUSE' AND PUT THE "VENTURE" AT RISK OF 'SANCTIONING ABUSE.'

See **Exhibit B.30** hereto attached.

7.31 OPINION – FORMULARY ACCESS IS KEY TO SALES - FORMULARY RESTRICTIONS HAD THE LARGEST INFLUENCE ON PRESCRIBING - PURDUE USED INFLUENCE TO GET OXYCONTIN ON MAYO CLINIC FORMULARY.

See **Exhibit B.31** hereto attached.

7.32 OPINION – GETTING ON THE FORMULARY IN OHIO WAS IMPORTANT TO JOHNSON & JOHNSON.

See **Exhibit B.32** hereto attached.

7.33 OPINION – THE BIG THREE DISTRIBUTOR DEFENDANTS USE GROUP PURCHASING ORGANIZATIONS (GPO'S).

See **Exhibit B.33** hereto attached.

7.34 OPINION – HARMS OF LAO FOR CHRONIC PAIN OUTWEIGH THE RISKS.

See **Exhibit B.34** hereto attached.

7.35 OPINION – IN 1997, PURDUE SECRETLY ACKNOWLEDGED THE ABUSE POTENTIAL OF OXYCONTIN. THEY EVEN KNEW THAT PATIENTS IN SHORT TERM STUDIES MANIFESTED BEHAVIOR SUSPICIOUS OF ADDICTION. PURDUE MARKETING SAID THE OPPOSITE CREATING ANTI-WARNINGS FALSELY REASSURING PRESCRIBERS THAT THE RISK OF ADDICTION WAS LOW OR ABSENT. IN ADDITION, PURDUE CHOSE TO NOT ESTABLISH A POST-MARKET ABUSE MONITORING SYSTEM TO EVALUATE THE EXTENT OF DIVERSION AND ADDICTION. PURDUE TREATED THE PRESCRIBERS AS MUSHROOMS.

See **Exhibit B.35** hereto attached.

7.36 OPINION – IN 2004 I TOLD PURDUE THEY WERE DOING ALL THESE BAD THINGS. THEY CONTINUED TO DO THEM AND WORSE

See **Exhibit B.36** hereto attached.

7.37 OPINION – FROM THE MID TO THE LATE 2000S, MARKETING SHIFTED TO INTEGRATED DELIVERY NETWORKS FROM INDIVIDUAL DOCTORS. AS A RESULT, DOCTORS ARE LOCKED INTO DRUG FORMULARIES.

See **Exhibit B.37** hereto attached.

7.38 OPINION – OPIOID PRODUCTS SHOULD HAVE INCLUDED THE FOLLOWING WARNINGS

See **Exhibit B.38** hereto attached.

7.39 OPINION – OPIOIDS ARE ADDICTIVE.

See **Exhibit B.39** hereto attached.

7.40 OPINION – PURDUE AND THE FDA CONCLUDED PALLADONE WAS LETHAL AND ITS RISKS OUTWEIGHED ITS BENEFITS BUT THEY DID NOT ISSUE A RECALL. PURDUE ISSUED RECALLS FOR DRUGS THAT WOULD NOT INJURE PATIENTS IF SOLD. THE NUMBER OF PATIENTS WHO DIED AS A RESULT IS UNKNOWN.

See **Exhibit B.40** hereto attached.

7.41 OPINION – PURDUE CLAIMS IT DISCONTINUED DISTRIBUTION OF 160 MG PILL IN APRIL 2001 BUT THIS REMAINED A DOSE IN THE LABEL. THUS, MEDICAL DOCTORS WOULD BE GIVEN THE MISIMPRESSION THAT 640 MG A DAY WAS AN APPROVED DOSE.

See **Exhibit B.41** hereto attached.

7.42 OPINION – PURDUE HIRED PROSTITUTES TO PROMOTE OXYCONTIN CR. THIS IS WRONG. PURDUE DISCUSSED VARIOUS WAYS TO CAPITALIZE ON SEX.

See **Exhibit B.42** hereto attached.

7.43 OPINION – PURDUE KNEW THAT OXYCONTIN HAD KILLED HUMAN BEINGS WHO TOOK INEFFECTIVE DOSES OF OXYCONTIN.

See **Exhibit B.43** hereto attached.

7.44 OPINION – PURDUE OXY CHAIN

See **Exhibit B.44** hereto attached.

7.45 OPINION – PURDUE USED SEX TO SELL. THIS IS WRONG.

See **Exhibit B.45** hereto attached.

7.46 OPINION – PURDUE VIOLATED ITS CIA

See **Exhibit B.46** hereto attached.

7.47 OPINION – SACKLER FRAUD BEGAN EARLY - SEE GLUTAVITE AD.

See **Exhibit B.47** hereto attached.

7.48 OPINION – THE WORDS DETAILED AND THOROUGH WERE DELIBERATELY REMOVED BY PURDUE FROM ITS ORDER MONITORING SYSTEM STANDARD OPERATING PROCEDURE AS PURDUE'S INTENT WAS NOT TO BE DETAILED AND THOROUGH.

See **Exhibit B.48** hereto attached.

7.49 OPINION – TEVA OFF LABEL MARKETING CREATED A REVERSE CORPORATE INTEGRITY AGREEMENT VIOLATION.

See **Exhibit B.49** hereto attached.

7.50 OPINION – TEVA OFF LABEL MARKETED TO NON-CANCER PATIENTS. CNMP PAIN IS NOT CANCER PAIN.

See **Exhibit B.50** hereto attached.

7.51 OPINION – THE "VENTURE" INFLUENCED WHO GUIDELINES AND THEN USED THEM TO UP SELL.

See **Exhibit B.51** hereto attached.

7.52 OPINION – THE "VENTURE" (INCLUDING TEVA) USED SEX TO SELL.

See **Exhibit B.52** hereto attached.

7.53 OPINION – THE FDA AGREES THAT THERE IS INSUFFICIENT EVIDENCE THAT THE RISK OF OPIOIDS OUTWEIGHS THE BENEFITS FOR TREATMENT OF CHRONIC NON-MALIGNANT PAIN.

See **Exhibit B.53** hereto attached.

7.54 OPINION – PATIENT SAVINGS CARD PROGRAMS BOTH INCREASE AND PROLONG THE USE OF OPIOIDS.

See **Exhibit B.54** hereto attached.

7.55 OPINION – WALGREENS CONTACTED OVER PRESCRIBING DOCTORS. THIS WAS A GOOD THING TO DO. TOO LITTLE TOO LATE HOWEVER.

See **Exhibit B.55** hereto attached.

7.56 OPINION – WALGREENS KNEW PHARMACISTS COULD MANIPULATE QUANTITIES WITH THE AS400 SOFTWARE AND THEY KNEW THIS COULD RESULT IN CRIMINAL NOT JUST CIVIL ACTIONS.

See **Exhibit B.56** hereto attached.

7.57 OPINION – ENDO, J&J, MALLINCKRODT AND TEVA AND PURDUE USED THE SAME COMPANY TO BUILD THEIR KEY OPINION LEADER (KOL) DATABASE.

See **Exhibit B.57** hereto attached.

7.58 OPINION – IN 2001, THE "VENTURE" WAS ON NOTICE ABOUT THE RISKS INHERENT IN SALE OF OPIOIDS FOR CHRONIC PAIN AND TOOK STEPS TO UNDERMINE WARNINGS ABOUT THESE RISKS. I AGREE WITH HOLMBERG.

See **Exhibit B.58** hereto attached.

7.59 OPINION – THE "VENTURE'S" "EVOLVED MESSAGE" WAS OR SHOULD HAVE BEEN KNOWN IN 1995.

See **Exhibit B.59** hereto attached.

7.60 OPINION –THE FDA NEGOTIATED A DEAL WITH ROXANE ALLOWING ROXANE TO MARKET 15 AND 30 IR BASED ON A 505 (B2) IN EXCHANGE FOR ROXANE'S AGREEMENT TO NOT SELL SR.

See **Exhibit B.60** hereto attached.

7.61 OPINION – OXYCONTIN DOSES ESCALATED RAPIDLY BECAUSE FOR MOST PATIENTS IT WAS NOT A 12 HOUR DRUG.

See **Exhibit B.61** hereto attached.

7.62 OPINION – WHEN THE FDA TRIED TO LIMIT USE IN 2001 BY CHANGING THE LABEL FROM "MORE THAN A FEW DAYS" TO "EXTENDED PERIOD OF TIME", THE "VENTURE" USED THIS LANGUAGE TO INCREASE THE MARKET.

See **Exhibit B.62** hereto attached.

7.63 OPINION – DOCTORS ON THE "VENTURE'S" PAYROLL ADMITTED THAT PSEUDOADDICTION DESCRIBES BEHAVIORS 'CLEARLY CHARACTERIZED AS DRUG ABUSE' AND PUT THE "VENTURE" AT RISK OF 'SANCTIONING ABUSE' WHICH THEY DID.

See **Exhibit B.63** hereto attached.

7.64 OPINION – DR. HADDOX AND PURDUE KNEW THAT PRESCRIBERS' PERCEPTION OF THE RISK OF OPIOIDS WITH RESPECT TO ABUSE AND ADDICTION AMONG CHRONIC PAIN PATIENTS SHOULD BE INCREASED TWOFOLD.

See **Exhibit B.64** hereto attached.

7.65 OPINION – THERE IS A DUTY TO MONITOR MARKETING.

See **Exhibit B.65** hereto attached.

7.66 OPINION – "VENTURE" DISTRIBUTOR ABC WORKED WITH MANUFACTURES TO MARKET OPIOIDS.

See **Exhibit B.66** hereto attached.

7.67 OPINION – FORMULARIES HAVE AN UNOFFICIAL "IF YOU ADD ONE YOU DELETE ONE" POLICY.

See **Exhibit B.67** hereto attached.

7.68 OPINION – THE "VENTURE" ACTED IN CONCERT TO EXPAND THE INDICATIONS FOR USE OF OPIOIDS TO TREAT DISEASES FOR WHICH OPIOIDS WERE NOT INDICATED AND INCREASE THE DAILY DOSE AND DURATION OF USE OF OPIOIDS AND INCREASE THE USE OF LONG ACTING OPIOIDS.

See **Exhibit B.68** hereto attached.

7.69 OPINION – THE "VENTURE" CORRUPTED THE FDA.

See **Exhibit B.69** hereto attached.

7.70 OPINION –FDA FAILED TO PROPERLY REGULATE OPIOID INDICATIONS. WHEN THE FDA TRIED TO LIMIT USE IN 2001 BY CHANGING THE LABEL FROM "MORE THAN A FEW DAYS" TO "EXTENDED PERIOD OF TIME", THE "VENTURE" USED THIS LANGUAGE TO INCREASE THE MARKET.

See **Exhibit B.70** hereto attached.

7.71 OPINION – THE "VENTURE" USED THE REVOLVING DOOR FDA-INDUSTRY TO GET FAVORABLE RULINGS TO ENABLE THEM TO EXPAND THE MARKET TO PATIENTS WHO THEY AND THE FDA KNEW WERE INAPPROPRIATE FOR LONG TERM NARCOTICS.

See **Exhibit B.71** hereto attached.

7.72 OPINION – THE HEAD OF THE DIVISION OF THE FDA RESPONSIBLE FOR OPIOIDS BEING APPROVED IS NOT A 'WATCHDOG' TO THE AMERICAN PEOPLE.

See **Exhibit B.72** hereto attached.

7.73 OPINION – THERE ARE FINANCIAL INTERLINKS BETWEEN THE WHOLESALERS (DISTRIBUTORS) AND EVERYONE ELSE IN THE CHAIN.

See **Exhibit B.73** hereto attached.

7.74 OPINION – THE "VENTURE" TARGETED VULNERABLE ELDERLY AND HAD TO CONVINCE DOCTORS TO USE OPIOIDS ON NURSING HOME PATIENTS.

See **Exhibit B.74** hereto attached.

7.75 OPINION – FORMULARY ACCESS IS KEY TO SALES.

See **Exhibit B.75** hereto attached.

7.76 OPINION – FORMULARY VERY IMPORTANT

See **Exhibit B.76** hereto attached.

7.77 OPINION – JANSSEN TARGETED YOUTH AND ATHLETES. JOHNSON & JOHNSON WAS PART OF PAIN COALITION WITH JANSSEN THAT TARGETED YOUTH. PAIN IS NOT A DISEASE. JOHNSON & JOHNSON AND JANSSEN ENGAGED IN ACTIONS TARGETED AT DIRECTLY INFLUENCING POTENTIAL PATIENTS AND CHILDREN.

See **Exhibit B.77** hereto attached.

7.78 OPINION – LIMITING THE INITIAL NUMBER OF PILLS DISPENSED REDUCES ABUSE. THE "VENTURE" SHOULD HAVE TOLD PRESCRIBERS THIS.

See **Exhibit B.78** hereto attached.

7.79 OPINION – THERE IS NO SCIENTIFICALLY AUTHORITATIVE ESTIMATE OF THE NUMBER OF PEOPLE WHO EXPERIENCE CHRONIC NON-MALIGNANT PAIN. THE ORIGINAL 100 MILLION NUMBER WAS A MYTH BASED ON A HARRIS POLL FUNDED BY ORTHO-MCNEIL. HERE IS NO AGREED DEFINITION OF "CHRONIC PAIN." PHONE AND OTHER SURVEYS CANNOT ASSESS THIS QUESTION. TO ASSESS THIS QUESTION, PHYSICIANS NEED TO INTERVIEW SUBJECTS TO DETERMINE IF THE "PAIN" IS CAUSED BY WORK, PSYCHIATRIC OR SOCIAL ISSUES OR OTHER ACTIVITY (SPORTS) VS AN EPIPHENOMENON OF A PHYSICAL INJURY. FOR EXAMPLE, NO STUDY HAS EVALUATED THE IMPACT OF PATIENTS ADDICTED TO OPIOIDS USING "PAIN COMPLAINTS" TO ACQUIRE OPIOIDS ON THE ESTIMATES. NO STUDY HAS EVALUATED THE CULTURAL DIFFERENCES RELATED TO THE GENERATION OF "PAIN" COMPLAINTS. COMPARE FOR EXAMPLE ISRAEL OR ITALY TO FINLAND.

See **Exhibit B.79** hereto attached.

7.80 OPINION – THE "VENTURE" HID THEIR FUNDING OF RESEARCH BY LAUNDERING THE MONEY THROUGH THIRD PARTIES.

See **Exhibit B.80** hereto attached.

7.81 OPINION – THE "VENTURE" SHOULD HAVE KNOWN THAT HIGHER DOSES KILL AND WARNED ABOUT THIS.

See **Exhibit B.81** hereto attached.

7.82 OPINION – THE "VENTURE'S" MARKETING INFLUENCES DOCTORS.

See **Exhibit B.82** hereto attached.

7.83 OPINION – MALLINCKRODT AND WALGREENS AGREEMENTS INCLUDE CO-MARKETING.

See **Exhibit B.83** hereto attached.

7.84 OPINION – MARKETING IMPACTS ON SALES.

See **Exhibit B.84** hereto attached.

7.85 OPINION: MCKESSON AND PURDUE CO-MARKETED PURDUE DRUGS

See **Exhibit B.85** hereto attached.

7.86 OPINION – MCKESSON PUSHED OXYCONTIN

See **Exhibit B.86** hereto attached.

7.87 OPINION – MS CONTIN AND OXYCONTIN HAVE A SIMILAR CHEMICAL MAKEUP AND SHOULD HAVE SIMILAR WARNINGS. A COMPARISON OF THE OXYCONTIN AND MS CONTIN PACKAGE INSERTS SHOW AN AFFIRMATIVE "UNDERWARNING" BY PURDUE OF THE HEALTH RISKS OF OXYCONTIN.

See **Exhibit B.87** hereto attached.

7.88 OPINION – PURDUE DESTROYED INFORMATIONAL MATERIALS.

See **Exhibit B.88** hereto attached.

7.89 OPINION – PURDUE KNEW THAT INAPPROPRIATE PATIENTS WERE GETTING OXYCONTIN.

See **Exhibit B.89** hereto attached.

7.90 OPINION – PURDUE'S INAPPROPRIATE MARKETING IS DESCRIBED HERE.

See **Exhibit B.90** hereto attached.

7.91 OPINION – WALGREENS DEVELOPED AN INTERVENTION FOR OVER PRESCRIBING MEDICAL DOCTORS IN 2013.

See **Exhibit B.91** hereto attached.

7.92 OPINION – WALGREENS GOOD FAITH DISPENSING POLICY PILOTS SHOW HIGH DOSE OPIATE PRESCRIBERS AVOIDING WALGREENS – SHIFT TO OTHER STORES.

See **Exhibit B.92** hereto attached.

7.93 OPINION – PURDUE AND WALGREENS CIRCUMVENTED A DOJ PLEA DEAL

See **Exhibit B.93** hereto attached.

7.94 OPINION – TEVA VIOLATIONS OF GOOD SALES AND MARKETING PRACTICES.

See **Exhibit B.94** hereto attached.

7.95 OPINION – WALGREENS BAD CONDUCT EXAMPLES.

See **Exhibit B.95** hereto attached.

7.96 OPINION – THE "VENTURE" GROSSLY MISLED DISTRIBUTORS AND PATIENTS WITH THE CLAIM THAT "FEAR OF ADDICTION IS EXAGGERATED" WITHOUT OFFERING SUPPORTING EVIDENCE.

See **Exhibit B.96** hereto attached.

7.97 OPINION – TITRATION IS THE KEY FOR A "BIGGER BONUS" FOR THE "VENTURE" EVEN IF IT MEANS "ESCALATING DOSAGE AND NUMBER OF TABLETS".

See **Exhibit B.97** hereto attached.

7.98 OPINION – IN THE ONLY LONG-TERM STUDY OF HIGH DOSE OPIOID RX THERE WERE HIGH RATES OF ADDICTION

See **Exhibit B.98** hereto attached.

7.99 OPINION – MARKETING WORKS FENTORA EXAMPLE RETURN ON INVESTMENT

See **Exhibit B.99** hereto attached.

7.100 OPINION – HEALTHCARE DISTRIBUTION MANAGEMENT ASSN (HDMA NOW HDA) WAS RESPONSIBLE FOR SALE OF UNAPPROVED OPIOIDS

See **Exhibit B.100** hereto attached.

7.101 OPINION – I AGREE WITH THE UNIVERSITY OF WASHINGTON SELF-ANALYSIS. THIS IS NOT ALWAYS THE CASE BUT IT WAS FOR THEM. "THEY SAY WHOEVER FUNDS YOUR ORGANIZATION OWNS IT!"

See **Exhibit B.101** hereto attached.

7.102 OPINION – IMMPACT HAD IMPACT

See **Exhibit B.102** hereto attached.

7.103 IMMPACT WAS "VENTURE'S" SUCCESSFUL EFFORT TO HAVE THE FDA ADOPT POOR EPIDEMIOLOGIC PRACTICES TO APPROVE OPIOIDS. IT WAS PAY TO PLAY AND PROBABLY VIOLATED ANT-TRUST LAWS AS WELL.

See **Exhibit B.103** hereto attached.

7.104 OPINION – IRONICALLY THE UNDER TREATMENT OF AFRICAN AMERICANS AND HISPANICS PROTECTED THEM FROM OPIOID DEATHS

See **Exhibit B.104** hereto attached.

7.105 OPINION – JANSSEN PARTICIPATED IN IMMPACT PAY TO PLAY PROGRAM

See **Exhibit B.105** hereto attached.

7.106 OPINION – JANSSEN VIOLATED ITS CORPORATE INTEGRITY AGREEMENT

See **Exhibit B.106** hereto attached.

7.107 OPINION – THE DOJ RECOGNIZED THAT WALGREENS' DIVERSION PROBLEMS STEMMING FROM ITS JUPITER, FL DISTRIBUTION CENTER, IMPACTED OHIO USERS

See **Exhibit B.107** hereto attached.

7.108 OPINION – MALLINCKRODT KNEW MARKETING INFLUENCED DOCTOR PRESCRIBING OF OPIOIDS

See **Exhibit B.108** hereto attached.

7.109 OPINION – MANUFACTURERS USED WHOLESALERS AS CONDUIT FOR MARKETING

See **Exhibit B.109** hereto attached.

7.110 OPINION – MCKESSON CONTROLLED MARKET SHARE OF VARIOUS OPIOIDS.

See **Exhibit B.110** hereto attached.

7.111 OPINION – MCKESSON PROVIDED THE "VENTURE" BANG FOR THE BUCK IN TERMS OF ENHANCED SALES.

See **Exhibit B.111** hereto attached.

7.112 OPINION – I AGREE WITH PURDUE'S ANALYSIS OF ITS MARKETING OBLIGATIONS. THEY VIOLATED THEM.

See **Exhibit B.112** hereto attached.

7.113 OPINION – THE "VENTURE" ENCOURAGED SALES REPS TO PUSH DOCTORS TO "INDIVIDUALIZE THE DOSE" TO INCREASE PATIENTS' DOSAGES OF OPIOIDS.

See **Exhibit B.113** hereto attached.

7.114 OPINION – THE "VENTURE" FOUND THAT MARKETING WAS ESPECIALLY IMPORTANT TO SELL HIGHER DOSES OF OPIOIDS, SO THE "VENTURE" SPECIFICALLY FOCUSED ON MARKETING HIGH-DOSE OPIOIDS.

See **Exhibit B.114** hereto attached.

7.115 OPINION – I AGREE WITH THE OIG EVALUATION OF PROMOTION OF PRESCRIPTION DRUGS THROUGH PAYMENTS AND GIFTS (OEI-01-90-00480; 8/91)

See **Exhibit B.115** hereto attached.

7.116 OPINION – IN 2000, OXYCONTIN WAS IN 89% OF THE FORMULARIES IN OHIO

See **Exhibit B.116** hereto attached.

7.117 OPINION – PALERMO – PURDUE ATTEMPTS TO SMOKE SCREEN THE FDA ABOUT RELEASE TIMES FOR OXYCONTIN.

See **Exhibit B.117** hereto attached.

7.118 OPINION – THE "VENTURE" USED FOOD AND "VOUCHERS" TO SELL – TEVA'S CEPHALON

See **Exhibit B.118** hereto attached.

7.119 OPINION – OPIOIDS ARE TOXIC.

See **Exhibit B.119** hereto attached.

7.120 OPINION – 3RD PARTY MARKETING IS MOST EFFECTIVE.

See **Exhibit B.120** hereto attached.

7.121 OPINION – AMERISOURCE BERGEN ("ABC") WANTED TO 'LOW KEY' (HIDE) ITS ASSOCIATION WITH PAIN CARE FORUM ("PCF").

See **Exhibit B.121** hereto attached.

7.122 OPINION – ALL MARKETING SHOULD HAVE STATED DISEASES AND INJURIES THAT ARE NOT 'MODERATE PAIN.'

See **Exhibit B.122** hereto attached.

7.123 OPINION – ALLERGAN DATA DOES NOT PROVIDE EVIDENCE THAT ALLERGAN'S OPIOIDS WORK FOR CHRONIC NON-MALIGNANT PAIN.

See **Exhibit B.123** hereto attached.

7.124 OPINION – ANY MARKETING OF ANY OPIOID FOR A SPECIFIC DISEASE IS "OFF LABEL".

See **Exhibit B.124** hereto attached.

7.125 OPINION – "VENTURE" MEMBER CEPHALON ENCOURAGED OVERUSE BY OFF LABEL MARKETING

See **Exhibit B.125** hereto attached.

7.126 OPINION – "VENTURE" MEMBER JANSSEN ENGAGED IN A VARIETY OF ACTIVITIES TO UNDERMINE RISK OF ADDICTION AND INCREASE USE IN PATIENT WHERE USE WAS NOT OR CONTRAINDICATED. THEY ALSO USED FRONT GROUPS TO ASSIST.

See **Exhibit B.126** hereto attached.

7.127 OPINION – "VENTURE" MEMBER JANSSEN (JOHNSON & JOHNSON) ENGAGED IN A VARIETY OF ACTIVITIES TO UNDERMINE RISK OF ADDICTION AND INCREASE INAPPROPRIATE USE. THEY ALSO USED FRONT GROUPS TO ASSIST.

See **Exhibit B.127** hereto attached.

7.128 OPINION – "VENTURE" MEMBER MALLINCKRODT MISREPRESENTED PROPER DOSING TO ITS SALES REPRESENTATIVES.

See **Exhibit B.128** hereto attached.

7.129 OPINION – "VENTURE" MEMBER MCKESSON MARKETED OPIOIDS.

See **Exhibit B.129** hereto attached.

7.130 OPINION – "VENTURE" MEMBER TEVA USED MARKETING TO UNDERMINE ADDICTION RISK AND MARKET DIRECTLY TO PATIENTS.

See **Exhibit B.130** hereto attached.

7.131 OPINION – COCHRANE EVALUATIONS DO NOT WORK FOR SIDE EFFECTS.

See **Exhibit B.131** hereto attached.

7.132 OPINION – CONTROL OF INAPPROPRIATE DISPENSING DID NOT IMPACT ON PATIENT NEED FOR PAIN CONTROL.

See **Exhibit B.132** hereto attached.

7.133 OPINION – CUYAHOGA COUNTY RELIED ON ITS PHARMACY BENEFIT MANAGER TO DETERMINE ITS FORMULARY.

See **Exhibit B.133** hereto attached.

7.134 OPINION – DEA ALERTED WALGREENS ABOUT IT'S BAD PRACTICES AND A PHARMACIST'S DUTY.

See **Exhibit B.134** hereto attached.

7.135 OPINION – DISTRIBUTOR MARKETING DROVE SALES.

See **Exhibit B.135** hereto attached.

7.136 OPINION – ENDO SOUGHT TO INFLUENCE FORMULARY DECISIONS BY FINDING PEOPLE TO INFLUENCE.

See **Exhibit B.136** hereto attached.

7.137 OPINION – ENDO WAS EITHER TOO CHEAP TO ADD ITS OPIOID LABELS TO THE 2014 PDR OR COMPLETELY IRRESPONSIBLE FOR THIS FAILURE TO WARN DOCTORS OF ANY DATA CONCERNING THESE DANGEROUS DRUGS.

See **Exhibit B.137** hereto attached.

7.138 OPINION – "VENTURE" DISTRIBUTORS MARKETED OPIOIDS FOR MANUFACTURERS.

See **Exhibit B.138** hereto attached.

7.139 OPINION – ROXANE DID NOT PROVIDE SOUND SCIENCE TO THE FDA.

See **Exhibit B.139** hereto attached.

7.140 OPINION – FDA APPROVALS WERE NOT BASED ON SOUND SCIENCE PROVIDED BY PURDUE. EVEN THE SACKLERS AND PURDUE AGREE. SELLERS OF OXYCODONE SHOULD HAVE WARNED ABOUT HIGHER BLOOD LEVELS IN PEOPLE OLDER THAN 65.

See **Exhibit B.140** hereto attached.

7.141 OPINION – FORMULARY ACCESS WAS CRUCIAL

See **Exhibit B.141** hereto attached.

7.142 OPINION – FORMULARY ACCESS WAS/IS KEY TO SALES.

See **Exhibit B.142** hereto attached.

7.143 OPINION – PURDUE'S DAVID HADDOX MADE MANY MISLEADING STATEMENTS TO THE PRESS, BLAMING THE VICTIM INSTEAD OF THE "VENTURE" FOR ADDICTION, MINIMIZING ADDICTION RISK, OVERDOSE RISK, OPIOIDS WERE SAFE AND EFFECTIVE [160 MG PILL AND PALLADONE REMOVED].

See **Exhibit B.143** hereto attached.

7.144 OPINION – I ADOPT ALL OF DR. SAPER'S ANALYSIS OF THE HISTORY OF THE ORIGINS OF THE OPIOID EPIDEMIC

See **Exhibit B.144** hereto attached.

7.145 OPINION – IN 1995, PURDUE AND ABBOTT KNEW THAT THERE WAS A PAIN CATEGORY BETWEEN MODERATE AND SEVERE BUT THEY NEVER DISCLOSED THIS.

See **Exhibit B.145** hereto attached.

7.146 OPINION – IN 2001, THE FDA TOLD PURDUE NOT TO MARKET OXYCONTIN FOR TREATMENT OF OSTEOARTHRITIS OR LOW BACK PAIN BY ORDERING THEM TO DELETE SPECIFIC MENTION OF THESE DISEASES FROM THE LABEL. PURDUE TURNED THIS ORDER ON ITS HEAD, USING THE CHANGE TO REMOVE ALL LIMITS TO PRESCRIBING FOR ANY DISEASE WHERE THE PATIENT HAD MODERATE TO SEVERE PAIN.

See **Exhibit B.146** hereto attached.

7.147 OPINION – JICK SOLICITED MONEY FROM PURDUE

See **Exhibit B.147** hereto attached.

7.148 OPINION – MARKETING TO FIRST GRADERS IS UNETHICAL AND DISGUSTING.

See **Exhibit B.148** hereto attached.

7.149 OPINION – DOCTORS RESPOND TO MARKETING MESSAGES AND INCREASE PRESCRIPTIONS.

See **Exhibit B.149** hereto attached.

7.150 OPINION – NO ONE KNOWS WHAT CHRONIC PAIN IS AND THE DEFINITION IS A MOVING TARGET. IT IS NOT A DISEASE.

See **Exhibit B.150** hereto attached.

7.151 OPINION – NONE OF THE "VENTURE" EVER PERFORMED TOXICOLOGY OR SAFETY TESTING ON OXYCODONE.

See **Exhibit B.151** hereto attached.

7.152 OPINION – ONE OR MORE OF PURDUE'S "REDER'S DOC[TOR]S" AT THE FDA WERE ON THE FDA OXYCONTIN LABEL REVIEW TEAM IN 2001.

See **Exhibit B.152** hereto attached.

7.153 OPINION – OXYCONTIN WAS NOT APPROVED FOR PERSISTENT PAIN.

See **Exhibit B.153** hereto attached.

7.154 OPINION – PAIN TREATMENTS WERE A "GAIN LEADER" FOR OTHER DRUG SALES.

See **Exhibit B.154** hereto attached.

7.155 OPINION – PHARMACIES COULD HAVE REDUCED THE OPIOID PROBLEM.

See **Exhibit B.155** hereto attached.

7.156 OPINION – PHYSICIANS HAD THE MISIMPRESSION THAT OXYCONTIN WAS LESS POTENT THAN MS CONTIN. INSTEAD OF CORRECTING, THIS PURDUE TOOK ADVANTAGE OF THIS IGNORANCE TO ENCOURAGE INAPPROPRIATE USE OF OPIOIDS.

See **Exhibit B.156** hereto attached.

7.157 OPINION – PURDUE AGREES THAT MARKETING INCREASES SALES.

See **Exhibit B.157** hereto attached.

7.158 OPINION – PURDUE AND MCKESSON WORKED IN CONCERT TO GET MISINFORMATION INTO THE STREAM OF COMMERCE.

See **Exhibit B.158** hereto attached.

7.159 OPINION – PURDUE AND WALGREENS CO-PROMOTED HYSINGLA EXTENDED RELEASE HYDROCODONE.

See **Exhibit B.159** hereto attached.

7.160 OPINION – PURDUE CLAIMED OXYCONTIN WAS EFFECTIVE HOWEVER DUE TO THE Q12 DOSING THIS TURNED OUT TO BE FALSE AND DOSE ESCALATION OCCURRED CREATING AN OPIOID ADDICTION MACHINE

See **Exhibit B.160** hereto attached.

7.161 OPINION – PURDUE CREATED DEMAND WITH WHOLESALERS.

See **Exhibit B.161** hereto attached.

7.162 OPINION – PURDUE DESTROYED DOCUMENTS.

See **Exhibit B.162** hereto attached.

7.163 OPINION – CARDINAL PROVIDED MARKETING TO MANUFACTURERS TO GET MESSAGES TO CVS.

See **Exhibit B.163** hereto attached.

7.164 OPINION – PURDUE DID NOT WANT TO REVEAL ITS BLAME THE VICTIM APPROACH TO ADDICTION FROM ITS DRUGS.

See **Exhibit B.164** hereto attached.

7.165 OPINION – PURDUE EXERTED INFLUENCE OVER NATIONAL ASSOCIATION OF STATE CONTROLLED SUBSTANCES AUTHORITIES (NASCSA).

See **Exhibit B.165** hereto attached.

7.166 OPINION – PURDUE FAILED TO CORRECT MISINFORMATION ABOUT OPIOIDS FOR HEADACHES.

See **Exhibit B.166** hereto attached.

7.167 OPINION – PURDUE HAD AN EARLY WARNINGS PROGRAM TO TRACK ADVERSE PUBLICITY. MOST OF THIS RELATED TO ABUSE ADDICTION ETC. PURDUE CREATED A PUBLIC RELATIONS PROGRAM TO RESPOND RATHER THAN AN INTENSIVE PROGRAM TO TRACK AND INFLUENCE DOCTORS TO STOP.

See **Exhibit B.167** hereto attached.

7.168 OPINION – PURDUE HAD TO DEVELOP AND MAINTAIN AN INTENSIVE MARKETING PROGRAM TO HOLD MARKET SHARE AFTER THE INTRODUCTION OF GENERICS.

See **Exhibit B.168** hereto attached.

7.169 OPINION – PURDUE ILLEGALLY MARKETED MS CONTIN FOR A YEAR WITHOUT APPROVAL.

See **Exhibit B.169** hereto attached.

7.170 OPINION – PURDUE KNEW (1997) - INCREASING STOCK LEVELS CAN FOSTER DEMAND.

See **Exhibit B.170** hereto attached.

7.171 OPINION – PURDUE KNEW DOCTORS WERE NOT USING OXY APPROPRIATELY.

See **Exhibit B.171** hereto attached.

7.172 OPINION – PURDUE KNEW THAT PRIMARY CARE DOCTORS CARRY OUT THE DAY TO DAY MANAGEMENT OF PAIN PATIENTS. HOWEVER CHRONIC OPIOID THERAPY SHOULD ONLY BE MANAGED BY DOCTORS WHO HAD EXPERT EXPERIENCE IN TREATING PATIENTS WITH OPIOIDS FOR CHRONIC PAIN. (SEE 2015 LABEL) THE LATTER GROUP MAY HAVE INCLUDED FEW PRIMARY CARE DOCTORS.

See **Exhibit B.172** hereto attached.

7.173 OPINION – PURDUE MADE MISLEADING CLAIMS ABOUT OXYCONTIN.

See **Exhibit B.173** hereto attached.

7.174 OPINION – PURDUE MARKETED MS CONTIN WITH FALSE AND MISLEADING CLAIMS AND IGNORED FDA CITATIONS TELLING THEM TO STOP.

See **Exhibit B.174** hereto attached.

7.175 OPINION – PURDUE MARKETED OXYCONTIN TO INAPPROPRIATE PATIENTS.

See **Exhibit B.175** hereto attached.

7.176 OPINION – PURDUE OFF LABEL MARKETED FOR ACUTE PAIN.

See **Exhibit B.176** hereto attached.

7.177 OPINION – PURDUE OFF LABEL MARKETED FOR MINOR PAIN.

See **Exhibit B.177** hereto attached.

7.178 OPINION – PURDUE OFF LABEL MARKETED FOR PATIENTS WHO SHOULD NOT HAVE BEEN TREATED WITH AN OPIOID.

See **Exhibit B.178** hereto attached.

7.179 OPINION – PURDUE PAID INDIVIDUALS TO PRESENT ON OPIOIDS.

See **Exhibit B.179** hereto attached.

7.180 OPINION – PURDUE PLANTED ARTICLES IN MEDIA TO UNDERMINE THE PUBLIC HEALTH RESPONSE TO THE OPIOID CRISIS. ASCH.ORG

See **Exhibit B.180** hereto attached.

7.181 OPINION – PURDUE PRESSURED PHARMACISTS TO SELL OXYCONTIN

See **Exhibit B.181** hereto attached.

7.182 OPINION – PURDUE REFUSED TO SPEND MONEY TO CHECK FOR SUSPICIOUS ORDERS.

See **Exhibit B.182** hereto attached.

7.183 OPINION – PURDUE REPLACES UNINSURED STOLEN OXY AND NATIONAL ACCOUNTS EDUCATED OVER 12,000 PHARMACISTS IN LIVE VENUES – ON THE "DUTY TO DISPENSE: "OVERCOMING UNCERTAINTY, DOUBT, AND FEAR."

See **Exhibit B.183** hereto attached.

7.184 OPINION – PURDUE SOUGHT TO HIDE INFORMATION ON MARKETING PITCHES AND RESPONSES. THIS VIOLATES THEIR OBLIGATION TO REPORT OVERUSE, PILL MILLS, ETC.

See **Exhibit B.184** hereto attached.

7.185 OPINION – PURDUE TRAINED WALGREENS PHARMACISTS.

See **Exhibit B.185** hereto attached.

7.186 OPINION – PURDUE USED FRONT GROUPS.

See **Exhibit B.186** hereto attached.

7.187 OPINION – PURDUE USED AMERICAN PAIN FOUNDATION (APF) TO UNDERMINE PROBLEMS RELATED TO ABUSE AND DIVERSION.

See **Exhibit B.187** hereto attached.

7.188 OPINION – PURDUE USED WHOLESALERS AND RETAILERS TO MARKET OPIOIDS.

See **Exhibit B.188** hereto attached.

7.189 OPINION – PURDUE WAS TRACKING DEATHS FROM OXYCONTIN BY 2000.

See **Exhibit B.189** hereto attached.

7.190 OPINION – PURDUE WORKED TO BLOCK DEA FROM RESTRICTING USE OF OPIOIDS TO PAIN SPECIALISTS. THIS WAS WRONG.

See **Exhibit B.190** hereto attached.

7.191 OPINION – PURDUE WORKED WITH MANAGED CARE ORGANIZATIONS AND USED REBATES TO DRIVE VOLUME. THIS IS CONCERTED ACTION TO DRIVE VOLUME.

See **Exhibit B.191** hereto attached.

7.192 OPINION – PURDUE'S ALLEGED ACTIONS TO ADDRESS ADDICTION WAS DRIVEN BY ITS DESIRE TO MAINTAIN MARKET SHARE AND UNDERMINE THE PUBLIC'S CONCERN ABOUT ADDICTION. THAT IS WHY PURDUE FOCUSED ITS EFFORTS ON BLAMING THE VICTIMS AND "CRIMINALS" RATHER THAN ITS OWN PRODUCT AND MARKETING PRACTICES.

See **Exhibit B.192** hereto attached.

7.193 OPINION – REBATES INCREASE PROFITS AND SALES AND WERE USED TO INFLUENCE PHARMACISTS.

See **Exhibit B.193** hereto attached.

7.194 OPINION – REINSTATEMENT REQUIRED BUYING CONDITIONS THAT WOULD INCREASE SALES.

See **Exhibit B.194** hereto attached.

7.195 OPINION – REVOLVING DOOR - DR. GOTTLEIB SUPPORTS IMMPACT WHILE INVESTING IN PHARMACEUTICAL COMPANIES AND THEN BECOMES HEAD OF FDA.

See **Exhibit B.195** hereto attached.

7.196 OPINION – RICHARD SACKLER IS THE PABLO ESCOBAR OF THE NEW MILLENNIUM. I AGREE.

See **Exhibit B.196** hereto attached.

7.197 OPINION – TARGET RELAXED GOOD FAITH DISPENSING IN 2014.

See **Exhibit B.197** hereto attached.

7.198 OPINION – THE AMERICAN PAIN FOUNDATION (APF) REPEATED THE "VENTURE'S" LIES THAT OPIOIDS ARE NOT ADDICTIVE IF TAKEN AS DIRECTED AND PROVIDE "RELIEF," NOT A "HIGH".

See **Exhibit B.198** hereto attached.

7.199 OPINION – THE "VENTURE" USED FRONT GROUPS TO INCREASE SALES. IN THIS CASE ABC INSTRUCTS ENDO ON HOW TO USE FRONT GROUPS.

See **Exhibit B.199** hereto attached.

7.200 OPINION – THE "VENTURE" AGGRESSIVELY MARKETED OPIOIDS AS DRUGS TO "START WITH AND STAY WITH" DESPITE KNOWLEDGE OF ITS ADDICTIVE NATURE.

See **Exhibit B.200** hereto attached.

7.201 OPINION – THE "VENTURE" AND FDA HAD OFF THE RECORD CONVERSATIONS TO COORDINATE POLICY DECISIONS. HADDOX REPRESENTS 22 COMPANIES

See **Exhibit B.201** hereto attached.

7.202 OPINION – THE "VENTURE" AND KEY OPINION LEADERS HELPED O'BRIEN REVISE THE DIAGNOSTIC AND STATISTICAL MANUAL (DSM) V TO CHANGE THE LANGUAGE OF THE OPIOID DISORDER FROM DEPENDENCE TO ADDICTION.

See **Exhibit B.202** hereto attached.

7.203 OPINION – THE "VENTURE" CHANGED THE DIAGNOSTIC AND STATISTICAL MANUAL (DSM) LANGUAGE TO GIVE THE IMPRESSION THAT ADDICTION WAS INHERENT AND THUS NOT A CRITERIA FOR DEPENDENCE.

See **Exhibit B.203** hereto attached.

7.204 OPINION – THE "VENTURE" CITES 'MOST DOCTORS' AS STATING THAT 'PATIENTS TREATED WITH PROLONGED OPIOID MEDICINES USUALLY DO NOT BECOME ADDICTED.' THERE IS NO EVIDENCE THAT 'MOST DOCTORS' SUPPORT THIS CLAIM.

See **Exhibit B.204** hereto attached.

7.205 OPINION – THE "VENTURE" COULD HAVE IMPACTED ON MISUSE THROUGH PHARMACY INTERVENTION – GOOD FAITH DISPENSING PROGRAM EXAMPLE WALGREENS

See **Exhibit B.205** hereto attached.

7.206 OPINION – THE "VENTURE" COULD HAVE TRACKED THE IMPACT OF ITS ACTIVITIES ON OFF-LABEL USE OF OPIOIDS. IT FAILED TO DO SO.

See **Exhibit B.206** hereto attached.

7.207 OPINION – THE "VENTURE" CREATED MISINFORMATION ON ADDICTION RISK AND TREATMENT INDICATIONS.

See **Exhibit B.207** hereto attached.

7.208 OPINION – THE "VENTURE" CREATED THE ENTITY KNOWN AS, 'PSEUDOADDICTION' SEPARATE FROM 'REAL ADDICTION' TO DOCTORS AND INSTRUCTED DOCTORS TO INCREASE OPIOID DOSES IN THESE SITUATIONS.

See **Exhibit B.208** hereto attached.

7.209 OPINION – THE "VENTURE" DID NOT USE THESE SURVEY METHODS TO TRY TO STOP OVERPRESCRIBING.

See **Exhibit B.209** hereto attached.

7.210 OPINION – THE "VENTURE" FOCUSED ON FORMULARY APPROVALS.

See **Exhibit B.210** hereto attached.

7.211 OPINION – THE "VENTURE" HAD AT LEAST 3 APPROACHES TO FORMULARY PENETRATION.

See **Exhibit B.211** hereto attached.

7.212 OPINION – THE "VENTURE" HAD A COMPLETE LACK OF UNDERSTANDING OF ADDICTION. ADDICTION IS NOT A CRIME. ADDICTION UNLIKE "CHRONIC PAIN" IS A DISEASE.

See **Exhibit B.212** hereto attached.

7.213 OPINION – THE "VENTURE" HAD A VARIETY OF APPROACHES TO INCREASE OPIOID USE.

See **Exhibit B.213** hereto attached.

7.214 OPINION – THE "VENTURE" HAS THE "SELLING TOOLS" TO "KEEP PATIENTS ON OXYCONTIN LONGER AND AT HIGHER DOSES."

See **Exhibit B.214** hereto attached.

7.215 OPINION – THE "VENTURE" HEALTHCARE DISTRIBUTION MANAGEMENT ASSN (HDMA/HDA) MEMBERSHIP.

See **Exhibit B.215** hereto attached.

7.216 OPINION – THE "VENTURE" INCLUDING DISTRIBUTORS MARKETED UNAPPROVED DRUGS.

See **Exhibit B.216** hereto attached.

7.217 OPINION – THE "VENTURE" INFLUENCED NIH CANCER PAIN MANAGEMENT HANDBOOK TO FACILITATE INCREASED USE OF OPIOIDS IN THIS CASE, ESPECIALLY ENDO'S PRODUCT.

See **Exhibit B.217** hereto attached.

7.218 OPINION – THE "VENTURE" INFLUENCED THE SELECTION OF THE PRESIDENT OF THE AMERICAN PAIN FOUNDATION.

See **Exhibit B.218** hereto attached.

7.219 OPINION – THE "VENTURE" INSTRUCTED ITS SALES REPS TO "EXTEND AVERAGE TREATMENT DURATION" TO MEET ITS GOAL OF $2.9B GROSS FUNDS IN 2010.

See **Exhibit B.219** hereto attached.

7.220 OPINION – THE "VENTURE" KNEW MARKETING TO DOCTORS WORKED.

See **Exhibit B.220** hereto attached.

7.221 OPINION – THE "VENTURE" KNEW MARKETING TO PHARMACISTS WORKED.

See **Exhibit B.221** hereto attached.

7.222 OPINION – THE "VENTURE" KNEW THAT PATIENTS AND DOCTORS WOULD CONSIDER TRIVIAL PAIN TO MERIT MODERATE TO SEVERE DESIGNATION INCLUDING INGROWN TOENAILS.

See **Exhibit B.222** hereto attached.

7.223 OPINION – THE "VENTURE" KNEW THAT THE JICK LETTER DID NOT EVALUATE USE OF OXYCONTIN. THEY HID THIS FROM MEDICAL DOCTORS AND THE PUBLIC.

See **Exhibit B.223** hereto attached.

7.224 OPINION – THE "VENTURE" MADE UNSUBSTANTIATED CLAIMS AND MINIMIZED ADDICTION RISK TO DOCTORS AND PATIENTS.

See **Exhibit B.224** hereto attached.

7.225 OPINION – THE "VENTURE" MISREPRESENTED THE DEFINITION OF ADDICTION BY STATING THAT "TAKING OPIOIDS FOR PAIN RELIEF IS NOT ADDICTION".

See **Exhibit B.225** hereto attached.

7.226 OPINION – THE "VENTURE" PAID CHARLES O'BRIEN, WHO WROTE THE SUBSTANCE USE DISORDER PORTION OF DIAGNOSTIC AND STATISTICAL MANUAL (DSM) V. O'BRIEN SAID HE COULD "DELAY INVOICING" UNTIL THE NEXT YEAR TO AVOID DISCLOSING THESE PAYMENTS.

See **Exhibit B.226** hereto attached.

7.227 OPINION – THE "VENTURE" RECOGNIZED THEY THERE WAS NO EVIDENCE THAT LONG TERM OPIOIDS WORKED BETTER THAN PLACEBO. THEY NEVER PERFORMED THIS STUDY.

See **Exhibit B.227** hereto attached.

7.228 OPINION – THE "VENTURE" REPEATEDLY ACKNOWLEDGED THEIR MAFIA STATUS AND EXPLAINED HOW THEY OPERATED.

See **Exhibit B.228** hereto attached.

7.229 OPINION – THE "VENTURE" SET UP AMERICAN PAIN FOUNDATION (APF) TO INCREASE SALES AND MISLEAD THE PUBLIC ABOUT RISKS AND BENEFITS AND A POPULATION THAT WAS 'UNTREATED'.

See **Exhibit B.229** hereto attached.

7.230 OPINION – THE "VENTURE" SOUGHT TO EXPAND SALES INAPPROPRIATELY.

See **Exhibit B.230** hereto attached.

7.231 OPINION – THE "VENTURE" TARGETED PHYSICIANS WHO DO NOT CONSIDER THEMSELVES PAIN EXPERTS IN ORDER TO INCREASE PRESCRIPTIONS.

See **Exhibit B.231** hereto attached.

7.232 OPINION – THE "VENTURE" TARGETED VULNERABLE POPULATIONS.

See **Exhibit B.232** hereto attached.

7.233 OPINION – THE "VENTURE" TOLD PHARMACIES THAT THERE WAS NO DOSE LIMIT. ADDICTION IS RELATED TO DOSE. THUS THIS MARKETING WAS AN ADDICTION CREATING MACHINE.

See **Exhibit B.233** hereto attached.

7.234 OPINION – THE "VENTURE" TRACKED MESSAGING. THEY KNEW WHO WAS CHEATING AND PUSHING PROMOTION MESSAGE RECALL DATA (PMRD).

See **Exhibit B.234** hereto attached.

7.235 OPINION – THE "VENTURE" TRAINED SALES REPS TO PUSH HIGH-DOSE OPIOIDS TO DOCTORS.

See **Exhibit B.235** hereto attached.

7.236 OPINION – THE "VENTURE" USE SEX TO SELL – ENDO.

See **Exhibit B.236** hereto attached.

7.237 OPINION – THE "VENTURE" USED AGGRESSIVE CONTROL TECHNIQUES TO INFLUENCE DOCTORS NOT EVIDENCE BASED MEDICINE.

See **Exhibit B.237** hereto attached.

7.238 OPINION – THE "VENTURE" USED AMERICAN PAIN FOUNDATION (APF) TO HIDE THE FUNDING SOURCE FOR TALKS.

See **Exhibit B.238** hereto attached.

7.239 OPINION – THE "VENTURE" USED AMERICAN PAIN SOCIETY (APS) AS A FRONT FOR MARKETING - "MULTI-ETHNIC STUDY = MARKETING".

See **Exhibit B.239** hereto attached.

7.240 OPINION – THE "VENTURE" USED BRIBES TO SELL.

See **Exhibit B.240** hereto attached.

7.241 OPINION – THE "VENTURE" USED FRONT GROUPS TO PROMOTE SALES TO WORK AROUND FDA MARKETING PROHIBITIONS.

See **Exhibit B.241** hereto attached.

7.242 OPINION – THE "VENTURE" USED FRONT GROUPS TO SECRETLY COMMUNICATE WITH EACH OTHER. FDA AND VORSANGER OF J&J GOT THIS.

See **Exhibit B.242** hereto attached.

7.243 OPINION – THE "VENTURE" USED PHARMACISTS TO INCREASE USE.

See **Exhibit B.243** hereto attached.

7.244 OPINION – THE "VENTURE" USED SEX TO SELL – PURDUE.

See **Exhibit B.244** hereto attached.

7.245 OPINION – THE "VENTURE" USED SEX TO SELL – MALLINCKRODT.

See **Exhibit B.245** hereto attached.

7.246 OPINION – THE "VENTURE" USED SEX TO SELL.

See **Exhibit B.246** hereto attached.

7.247 OPINION – THE "VENTURE" USED THE JOINT COMMISSION ON ACCREDITATION OF HEALTHCARE ORGANIZATIONS (JCAHO) PROCESS TO INCREASE USE OF OPIOIDS.

See **Exhibit B.247** hereto attached.

7.248 OPINION – THE "VENTURE" USED THE OPIOID POST-MARKETING REQUIREMENT CONSORTIUM (OPC) TO GENERATE FAVORABLE RESULTS, SECRETLY GHOST WRITE PAPERS ALL WITH PURPOSE OF INCREASING SALES BY MINIMIZING RISKS AND INCREASING THE POPULATION TARGETED FOR USE.

See **Exhibit B.248** hereto attached.

7.249 OPINION – THE "VENTURE" USED UNBRANDED MESSAGING TO PROMOTE SALES TO WORK AROUND FDA MARKETING PROHIBITIONS.

See **Exhibit B.249** hereto attached.

7.250 OPINION – THE "VENTURE" USED 'HOOKERS, STRIPPERS AND LAP DANCERS' AS ROUTINE SALES TECHNIQUES.

See **Exhibit B.250** hereto attached.

7.251 OPINION – THE "VENTURE" USED "EDUCATIONAL" LISTSERV PAIN_CHEM_DEP TO FIND HIGH-PRESCRIBING DOCTORS TO SELL ITS OPIOIDS.

See **Exhibit B.251** hereto attached.

7.252 OPINION – THE "VENTURE" DID NOT EMPHASIZE THE DIAGNOSES THAT ARE NOT MODERATE PAIN FOR OPIOIDS.

See **Exhibit B.252** hereto attached.

7.253 OPINION – THE FDA ORDERED OPANA ER REMOVED FROM THE MARKET JUNE 8 2017. ENDO DID NOT ISSUE A RECALL.

See **Exhibit B.253** hereto attached.

7.254 OPINION – THE JICK LETTER PROVIDED NO RELIABLE EVIDENCE ON THE RISK OF ADDICTION FROM OPIOID USE.

See **Exhibit B.254** hereto attached.

7.255 OPINION – THE PURDUE MARKETING PLAN TARGETED 100,000 MEDICAL DOCTORS AND 25,000 PHARMACY AND THERAPEUTICS (P&T) MEMBERS. THERE ARE NOT 100,000 MEDICAL DOCTORS WHO HAVE EXPERIENCE TREATING CHRONIC PAIN WITH OPIOIDS. THIS EXPANDED THE USE TO MEDICAL DOCTORS WHO SHOULD NOT HAVE PRESCRIBED THE DRUG.

See **Exhibit B.255** hereto attached.

7.256 OPINION – THE WHOLESALERS WERE A CONDUIT FOR MISINFORMATION TO PHARMACIES AND HAD THE CAPACITY TO MONITOR USE AND FAILED TO DO SO.

See **Exhibit B.256** hereto attached.

7.257 OPINION – TITRATION IS THE KEY FOR A 'BIGGER BONUS' FOR THE "VENTURE" EVEN IF IT MEANS 'ESCALATING DOSAGE AND NUMBER OF TABLETS'.

See **Exhibit B.257** hereto attached.

7.258 OPINION – TO INCREASE SALES, THE "VENTURE" USED PRESCRIBER DATA FROM IMS TO TARGET TO HIGH-PRESCRIBING PHYSICIANS INSTEAD OF TRACKING PATTERNS OF ABUSE.

See **Exhibit B.258** hereto attached.

7.259 OPINION – THE DEA DIDN'T BUY WAG'S ELECTRONIC RECORD ARGUMENT AND THREATENED WALGREENS WITH VIOLATIONS FOR EACH INSTANCE.

See **Exhibit B.259** hereto attached.

7.260 OPINION – WALGREENS AND PURDUE SHARED DATA.

See **Exhibit B.260** hereto attached.

7.261 OPINION – WALGREENS ANTICIPATED JUPITER SHUT DOWN AND DEVELOPED A WORK AROUND TO CIRCUMVENT DOJ AGREEMENT.

See **Exhibit B.261** hereto attached.

7.262 OPINION – WALGREENS GOOD FAITH WAS DONE IN RESPONSE TO DEA ACTION.

See **Exhibit B.262** hereto attached.

7.263 OPINION – WALGREENS KEPT SUBOXONE OFF OF FORMULARIES.

See **Exhibit B.263** hereto attached.

7.264 OPINION – WALGREENS PHARMACIES SOLD OUTRAGEOUS AMOUNTS OF OPIOIDS II.

See **Exhibit B.264** hereto attached.

7.265 OPINION – WALGREENS SOLD OUTRAGEOUS AMOUNTS OF OXY TO CERTAIN STORES.

See **Exhibit B.265** hereto attached.

7.266 OPINION – WALGREENS USED A FRONT AMERICAN ACADEMY OF PAIN MEDICINE (AAPM) TO MAKE IT APPEAR THAT ITS GOOD FAITH DISPENSING (GFD) PROGRAM WAS GOOD. THE FRONT MADE CHANGES TO UNDERMINE THE EFFICACY OF THE SYSTEM.

See **Exhibit B.266** hereto attached.

7.267 OPINION – WALGREENS USED A FRONT TO MAKE IT APPEAR THAT ITS GOOD FAITH DISPENSING (GFD) PROGRAM WAS GOOD.

See **Exhibit B.267** hereto attached.

7.268 OPINION – WHEN MADE AWARE OF PILL MILLS PURDUE DEVELOPED A PR STRATEGY TO DEFEND ITS PRODUCT RATHER THAN A PUBLIC HEALTH STRATEGY TO PROTECT PATIENTS.

See **Exhibit B.268** hereto attached.

7.269 OPINION – WHEN MADE AWARE OF PILL MILLS, PURDUE DEVELOPED STRATEGY TO UNDERMINE REGULATORY EFFORTS TO DEAL WITH THE PROBLEM.

See **Exhibit B.269** hereto attached.

7.270 OPINION – WHOLESALERS WORKED IN CONCERT WITH MANUFACTURERS TO PROMOTE OPIOID USE.

See **Exhibit B.270** hereto attached.

7.271 OPINION –THE "VENTURE" INFLUENCED THE NIH HANDBOOK ON CANCER PAIN TREATMENT AND USED IT TO INCREASE SALES.

See **Exhibit B.271** hereto attached.

7.272 OPINION –THE "VENTURE" USED FRONT GROUPS TO ENHANCE SALES BY UNDERMINING ADDICTION RISK AND EXPANDING USE AND INFLUENCING REGULATORS. THE "VENTURE" USED THE FRONT GROUPS TO MARKET DIRECTLY TO CONSUMERS.

See **Exhibit B.272** hereto attached.

7.273 OPINION – AMERICAN PAIN SOCIETY (APS), AMERICAN PAIN FOUNDATION (APF) AND OTHER PAIN SOCIETIES WERE FRONTS FOR THE "VENTURE". "UNCONDITIONAL GRANTS" WERE CONDITIONED ON THE CONDITION THAT THE PAIN SOCIETIES DID THE "VENTURE'S" BIDDING.

See **Exhibit B.273** hereto attached.

7.274 OPINION – THE "VENTURE" EXPANDED THE MARKET BY PROMOTING INAPPROPRIATE USE (LOW BACK SPASM) OF 3 YEARS DURATION WITH "SOME PAIN".

See **Exhibit B.274** hereto attached.

7.275 OPINION – THE "VENTURE" PUSHED LONG ACTING NARCOTICS FOR INITIAL DRUG PRESCRIPTION FOR ANY CAUSE OF PAIN INCREASING ADDICTION

See **Exhibit B.275** hereto attached.

7.276 OPINIONS - THE "VENTURE" PUSHED Q12 RATHER THAN INCREASING DOSE FREQUENCY INCREASING ADDICTION.

See **Exhibit B.276** hereto attached.

7.277 OPINIONS: THE SACKLER FAMILY ORIGINATED DIRECT-TO-CONSUMER DRUG MARKETING. THIS PRACTICE HAS SINCE BEEN WIDELY ADOPTED BY THE PHARMACEUTICAL AND MEDICAL DEVICE INDUSTRY.

See **Exhibit B.277** hereto attached.

7.278 THERE WAS PURDUE SPOLIATION.

See **Exhibit B.278** hereto attached.

7.279 OPINION – WALGREENS AND JUPITER MISCONDUCT – CORRECT MONITORING AND ACTIVELY CHANGING ORDERS TO AVOID REPORTING.

See **Exhibit B.279** hereto attached.

7.280 OPINION – PURDUE KNEW REBATES DROVE SALES.

See **Exhibit B.280** hereto attached.

7.281 OPINION – THE "VENTURE" HAD MANY SALES CODE VIOLATIONS – ENDO EXAMPLE

See **Exhibit B.281** hereto attached.

7.282 OPINION – PURDUE HAD A REBATE PROGRAM WITH PRIME THERAPEUTICS.

See **Exhibit B.282** hereto attached.

7.283 OPINION – THE "VENTURE" RELIED UPON A PSEUDO SYNDROME CALLED PSEUDOADDICTION, WHICH WAS USED BY THE "VENTURE" TO CONVINCE DOCTORS THAT PATIENTS WITH ADDICTION SYMPTOMS WERE NOT ACTUALLY ADDICTED TO OPIOIDS BUT RATHER NEEDED TO BE TREATED WITH EVER ESCALATING DOSES. A DIAGNOSIS OF PESUDOADDICTION WORSENED THE ADDICTION AND DELAYED OR BLOCKED TREATMENT FOR ADDICTION. THIS IS NOT EVIDENCE BASED MEDICINE.

See **Exhibit B.283** hereto attached.

7.284 OPINION – PURDUE EDITED THE AMERICAN MEDICAL DIRECTORS ASSOCIATIONS GUIDELINE FOR CHRONIC PAIN MANAGEMENT IN THE LONG-TERM CARE SETTING.

See **Exhibit B.284** hereto attached.

7.285 OPINION – PURDUE HAD A GROSS MISUNDERSTANDING OF HOW SCIENCE WORKS AND EPIDEMIOLOGY AND STATISTICS. THE FIRST RULE OF SCIENCE IS REPETITION OF EXPERIMENTS.

See **Exhibit B.285** hereto attached.

7.286 OPINION – THE "VENTURE" INFLUENCED PRACTITIONERS EXPLOITING OVER PRESCRIBERS AND FAILING TO REPORT MDS WHOSE PRESCRIBING LED TO DIVERSION

See **Exhibit B.286** hereto attached.

7.287 OPINION – PURDUE MANIPULATED SUSPICIOUS ORDER MONITORING ("SOM") BY MANIPULATING THE QUOTA SYSTEM

See **Exhibit B.287** hereto attached.

7.288 OPINION PURDUE MARKETED PAIN TREATMENT TO ELEMENTARY SCHOOL CHILDREN

See **Exhibit B.288** hereto attached.

7.289 OPINION PURDUE PRESENTED DATA TO THEIR SALES REPS IN THE OXYCONTIN LAUNCH MEETING THAT THE FDA SAID WOULD BE MISLEADING.

See **Exhibit B.289** hereto attached.

7.290 OPINION – IN 2013, STEPHEN SEID, PURDUE'S VP OF NATIONAL ACCOUNTS BROUGHT PRESSURE ON WALGREENS ABOUT GOOD FAITH DISPENSING (GFD).

See **Exhibit B.290** hereto attached.

7.291 OPINION – PURDUE REBATES TO WALGREENS BEGAN NO LATER THAN 1998.

See **Exhibit B.291** hereto attached.

7.292 OPINION – PURDUE REMOVED DETAILED AND THOROUGH FROM REVIEW OF ABUSE DATA.

See **Exhibit B.292** hereto attached.

7.293 OPINION – PURDUE SOLD AN UNSAFE OPIOID FOR ABOUT A YEAR BUT DID NOT ISSUE A RECALL.

See **Exhibit B.293** hereto attached.

7.294 OPINION – PURDUE MARKETED TO DENTISTS - THIS IS OFF LABEL.

See **Exhibit B.294** hereto attached.

7.295 OPINION – PURDUE TRAINED WALGREENS PERSONNEL IN NARCOTICS

See **Exhibit B.295** hereto attached.

7.296 OPINION – PURDUE TRIED TO INFLUENCE OHIO REGULATORY AGENCIES.

See **Exhibit B.296** hereto attached.

7.297 OPINION – PURDUE WANTED TO RETAIN THE POWER TO SLOW THE PUBLIC HEALTH RESPONSE TO THE OPIOID CRISIS.

See **Exhibit B.297** hereto attached.

7.298 OPINION – REBATES DRIVE SALES OF HIGHER DOSE OPIOIDS.

See **Exhibit B.298** hereto attached.

7.299 OPINION – WHOLESALER PERFORMANCE AGREEMENT BETWEEN PURDUE AND CARDINAL WAS A CONCERTED ACTION TO SELL AND PROMOTE OPIOIDS.

See **Exhibit B.299** hereto attached.

7.300 OPINION – 'CHRONIC NON-MALIGNANT PAIN' CAN BE A FUNCTION OF PHYSICAL WORK AND THUS SOCIOECONOMIC STATUS. THAT PAIN IS EITHER "NORMAL" OR SHOULD BE TREATED WITH CHANGES IN WORK. THE OVERWHELMING MAJORITY OF INDIVIDUALS, INCLUDING BUT NOT LIMITED TO, TEACHERS, RETAIL WORKERS, WAITRESSES, BARBERS, JANITORS, GARBAGE COLLECTORS, AND ATHLETES, DEVELOP CHRONIC NON-MALIGNANT PAIN.

See **Exhibit B.300** hereto attached.

7.301 OPINION – NATIONAL INITIATIVE ON PAIN CONTROL (NIPC) (ENDO) ALLOWED OFF LABEL MARKETING

See **Exhibit B.301** hereto attached.

7.302 OPINION – THE "VENTURE" HAD A COMPREHENSIVE PROGRAM TO PUSH OPIOIDS INCLUDING PUSHING DIRECT-TO-CONSUMER (DTC) AND TO INEXPERIENCED PRESCRIBERS

See **Exhibit B.302** hereto attached.

7.303 OPINION – "VENTURE" KEY OPINION LEADERS (KOLS) SEED THE LITERATURE WITHOUT DISCLOSING INDUSTRY FUNDING

See **Exhibit B.303** hereto attached.

7.304 OPINION – OXYCODONE IS UP TO 3 TIMES MORE POTENT THAN PREVIOUSLY ACKNOWLEDGED BY THE "VENTURE"

See **Exhibit B.304** hereto attached.

7.305 OPINION – THE "VENTURE" CHANGED DIAGNOSTIC AND STATISTICAL MANUAL (DSM) ADDICTION CRITERIA

See **Exhibit B.305** hereto attached.

7.306 OPINION – PURDUE COULD HAVE STOPPED THIS BY TRACKING IMS DATA LIKE THEY DID WITH ME. DENTAL USE SHOULD HAVE TRIGGERED AN INTERVENTION

See **Exhibit B.306** hereto attached.

7.307 OPINION – PURDUE TARGETED OHIO

See **Exhibit B.307** hereto attached.

7.308 OPINION – PURDUE TOLD ITS PERSONNEL NOT TO REPORT GENERAL ASSERTIONS OF DIVERSION

See **Exhibit B.308** hereto attached.

7.309 OPINION – SUMMIT COUNTY RELIED ON EXPRESSMEDS AND EXPRESS SCRIPTS FOR ITS FORMULARY

See **Exhibit B.309** hereto attached.

7.310 OPINION – TEVA OFF LABEL MARKETED ACTIQ

See **Exhibit B.310** hereto attached.

7.311 OPINION – THE 5TH VITAL SIGN WAS OPPOSED BY MEMBERS OF JOINT COMMISSION ON ACCREDITATION OF HEALTHCARE ORGANIZATIONS (JACHO). IT INCREASED ADDICTION RATES

See **Exhibit B.311** hereto attached.

7.312 OPINION – THE "VENTURE" CHANGED THE STANDARD OF CARE FOR PAIN TREATMENT WITHOUT EVIDENCE THAT THE CHANGE WOULD IMPROVE CARE BUT WITH EVIDENCE THAT THE CHANGE WOULD INCREASE PROFITS AND USE OF OPIOIDS

See **Exhibit B.312** hereto attached.

7.313 OPINION – THE "VENTURE" CREATES A MYTHICAL PROBLEM CALLED "UNDERTREATED PAIN" AND USED THAT MYTH TO FLOOD THE US MARKET WITH THE "OPIOIDS" SOLUTION.

See **Exhibit B.313** hereto attached.

7.314 OPINION – THE "VENTURE" KNEW PUSHING OPIOIDS WORKED

See **Exhibit B.314** hereto attached.

7.315 OPINION – THE "VENTURE" KNEW THE JICK LETTER DID NOT ADDRESS RISK OF ADDICTION FOR OPIOID TREATMENT OF CHRONIC NON-MALIGNANT PAIN (CNMP) BUT REFUSED TO FUND A MORE COMPREHENSIVE STUDY

See **Exhibit B.315** hereto attached.

7.316 OPINION – THE "VENTURE" MEMBERS HELPED PROMOTE USE OF OPIOIDS.

See **Exhibit B.316** hereto attached.

7.317 OPINION – THE "VENTURE" USED MIDDLE MEN AKA "PROFESSIONAL SOCIETIES" TO HIDE PAYMENTS TO SPEAKERS

See **Exhibit B.317** hereto attached.

7.318 OPINION – THE "VENTURE" GENERATED MEDICAL LITERATURE TO ENHANCE SALES

See **Exhibit B.318** hereto attached.

7.319 OPINION – THE RISK OF ADDICTION FROM LONG ACTING OPIOIDS (LAOS) IS UNKNOWN. TELLING PRESCRIBER THE RISK IS LOW OR RARE IS AN ANTI-WARNING THAT IS NOT BASED ON SCIENTIFIC EVIDENCE.

See **Exhibit B.319** hereto attached.

7.320 OPINION – THE "VENTURE" ACTED TOGETHER TO PASS LEGISLATIVE BILL S. 483, WHICH HINDERS THE DEA'S ABILITY TO INTERVENE IN SUSPICIOUS SHIPMENTS OF OPIOIDS.

See **Exhibit B.320** hereto attached.

7.321 OPINION – THE "VENTURE" – MCKESSON'S SUSPICIOUS ORDER MONITORING (SOM) WAS INADEQUATE.

See **Exhibit B.321** hereto attached.

7.322 OPINION – WALGREENS GOT AROUND SUSPICIOUS ORDER ISSUES - OTHER WHOLESALERS STEPPED IN.

See **Exhibit B.322** hereto attached.

7.323 OPINIONS – PURDUE RESPONSE TO MONITORING WAS INADEQUATE.

See **Exhibit B.323** hereto attached.

7.324 OPINION – AMERISOURCE BERGEN ("ABC") WAS LIGHT ON ORDER MONITORING. THE ABC FOCUS IS ONLY ON RAPID GROWTH, NOT STEADY SALES. FOCUS ON BIG ACCOUNTS ONLY FOR SUSPICIOUS ORDER MONITORING.

See **Exhibit B.324** hereto attached.

7.325 OPINION – MANUFACTURERS AND WHOLESALERS COORDINATED ACTIVITIES.

See **Exhibit B.325** hereto attached.

7.326 OPINION – PURDUE SPENT LESS THAN 2 MINUTES REVIEWING SUSPICIOUS ORDERS.

See **Exhibit B.326** hereto attached.

7.327 OPINION –WALGREENS CIRCUMVENTED ITS OWN POLICY TO AVOID ITS OBLIGATION TO INVESTIGATE AND REPORT SUSPICIOUS ORDERS.

See **Exhibit B.327** hereto attached.

7.328 OPINION – THE "VENTURE" IGNORED WARNINGS OF EXCESS DRUG SALES.

See **Exhibit B.328** hereto attached.

7.329 OPINION – "VENTURE" MEMBERS HAD AGREEMENTS WITH AUTHORIZED DISTRIBUTORS WHEREBY THEY RECEIVED DATA THAT COULD HAVE BEEN USED TO MONITOR SUSPICIOUS ORDERS. THIS DATA GAVE "VENTURE" MEMBERS VISIBILITY INTO THEIR CUSTOMER'S CUSTOMERS.

See **Exhibit B.329** hereto attached.

7.330 OPINION – THE "VENTURE" HAD DATA THAT COULD BE USED DO SUSPICIOUS ORDER MONITORING (SOM) BUT THEY DID NOT USE IT.

See **Exhibit B.330** hereto attached.

7.331 OPINION – WALGREENS HAD TO WORK HARD TO CIRCUMVENT CARDINAL RED FLAGGED STORES.

See **Exhibit B.331** hereto attached.

7.332 OPINION – WALGREENS SOFTWARE WAS AN EASY WORK AROUND CONTROLS.

See **Exhibit B.332** hereto attached.

7.333 OPINION – WALGREENS UNDERMINED ITS OWN SUSPICIOUS ORDER MONITORING (SOM) POLICY.

See **Exhibit B.333** hereto attached.

7.334 OPINION – WALGREENS USED MONITORING TO INCREASE RATHER THAN REDUCE ABUSE.

See **Exhibit B.334** hereto attached.

7.335 OPINION – WALGREENS REFUSED TO LET MANUFACTURERS AND WHOLESALERS AUDIT SUSPICIOUS ORDER MONITORING (SOM).

See **Exhibit B.335** hereto attached.

7.336 OPINION – MANUFACTURERS AND WHOLESALERS WERE CONNECTED AT THE HIP.

See **Exhibit B.336** hereto attached.

7.337 OPINION – THE "VENTURE" ACTED IN CONCERT TO TARGET INAPPROPRIATE PRESCRIBERS THAT IS PRESCRIBERS WHO ARE NOT "KNOWLEDGEABLE IN THE USE OF POTENT OPIOIDS FOR THE MANAGEMENT OF CHRONIC PAIN."

See **Exhibit B.337** hereto attached.

7.338 OPINION – THE "VENTURE" AIMED TO EXPAND THE INDICATIONS OF OPIOID ANALGESICS TO TREAT NON-CANCER PAIN SPECIFICALLY FOR TREATMENT OF CHRONIC PAIN AND IN PEDIATRIC POPULATIONS.

See **Exhibit B.338** hereto attached.

7.339 OPINION – THE "VENTURE" COOKED THE BOOKS.

See **Exhibit B.339** hereto attached.

7.340 OPINION – THE "VENTURE" KNEW THE 12 HOUR CLAIM WAS BOGUS.

See **Exhibit B.340** hereto attached.

7.341 OPINION – THE "VENTURE" LEVERAGED THE AMERICAN ACADEMY OF PAIN MEDICINE (AAPM) AND AMERICAN PAIN SOCIETY (APS) TO ADVERTISE NON-CANCER USE OF MS CONTIN TO DOCTORS, APPROVED BY THE FDA.

See **Exhibit B.341** hereto attached.

7.342 OPINION – THE "VENTURE" MARKETED DIRECTLY TO PHARMACIES.

See **Exhibit B.342** hereto attached.

7.343 OPINION – PURDUE MARKETED TO PHYSICIANS WHO WERE NOT "KNOWLEDGEABLE IN THE USE OF POTENT OPIOIDS FOR THE MANAGEMENT OF CHRONIC PAIN."FROM LABEL:

See **Exhibit B.343** hereto attached.

7.344 OPINION – THE "VENTURE" ORGANIZED LOBBYING.

See **Exhibit B.344** hereto attached.

7.345 OPINION – THE "VENTURE" OVER PROMOTED NARCOTICS.

See **Exhibit B.345** hereto attached.

7.346 OPINION – THE "VENTURE" PUSHED HIGHER DOSES THUS INCREASING ADDICTION.

See **Exhibit B.346** hereto attached.

7.347 OPINION – THE "VENTURE" PUSHED NARCOTICS FOR PATIENT WHO SHOULD NOT GET THEM I.E. PATIENTS WITH DISEASES THAT ARE BETTER TREATED WITH DRUGS FOR THEIR DISEASE (OSTEOARTHRITIS) OR TO DOCTORS WHO SHOULD NOT USE THEM (FAMILY PRACTITIONERS, REHABILITATION PHYSICIANS, AND NEUROLOGISTS).

See **Exhibit B.347** hereto attached.

7.348 OPINION – PURDUE PUSHED NO CEILING DOSE FOR OXYCONTIN INCREASING ADDICTION. THE MS CONTIN PUBLIC PERCEPTION OF END OF LIFE TREATMENT DOES NOT ACCOUNT FOR THE FACT THAT OXYCONTIN CAUSED PATIENT DEATHS.

See **Exhibit B.348** hereto attached.

7.349 OPINION – THE "VENTURE" INFLUENCED THE FDA RISK EVALUATION AND MITIGATION STRATEGY (REMS) PROGRAM.

See **Exhibit B.349** hereto attached.

7.350 OPINION – THE "VENTURE" SOUGHT TO INFLUENCE INTERNATIONAL ORGANIZATIONS

See **Exhibit B.350** hereto attached.

7.351 OPINION – THE "VENTURE" SOUGHT TO USE FRONT GROUPS TO INCREASE USE.

See **Exhibit B.351** hereto attached.

7.352 OPINION – THE "VENTURE" TRAINED SALES REPRESENTATIVES TO ABUSE THE TRUST OF DOCTORS TO SELL DRUGS.

See **Exhibit B.352** hereto attached.

7.353 OPINION – THE "VENTURE" USED DOSING TO ADDICT PATIENTS.

See **Exhibit B.353** hereto attached.

7.354 OPINION – THE "VENTURE" USED FORMULARY ACCESS TO INCREASE USE.

See **Exhibit B.354** hereto attached.

7.355 OPINION – THE "VENTURE" USED J&J LAWYER ANGAROLA TO INCREASE OPIOID USE

See **Exhibit B.355** hereto attached.

7.356 OPINION – THE "VENTURE" INFLUENCED THE MANAGED CARE MARKET TO INCREASE SALES - RELATIONSHIP BETWEEN THE MANUFACTURERS AND PHYSICIANS, PATIENTS, AND PHARMACISTS.

See **Exhibit B.356** hereto attached.

7.357 OPINION – THE "VENTURE" SOUGHT TO ADDICT VENERABLE POPULATIONS. REPS WERE PAID TWICE THE BONUS DOLLARS FOR LANDING A NURSING HOME, HOME HEALTH AND HEALTH AID VS A HOSPITAL OR PAIN CENTER.

See **Exhibit B.357** hereto attached.

7.358 OPINION – THE "VENTURE'S" EFFORTS TO KEEP KEY INFORMATION ON THE HARMFUL EFFECTS OF THEIR PRODUCTS A SECRET, THEIR ILLEGAL ACTS SECRET HAS MADE THE ADDICTION, ABUSE, AND OVERDOSE PROBLEM WORSE.

See **Exhibit B.358** hereto attached.

7.359 OPINION – THE "VENTURE" MARKETED TO INAPPROPRIATE PRESCRIBERS.

See **Exhibit B.359** hereto attached.

7.360 OPINION – THE "VENTURE" USED A VARIETY OF SALES TECHNIQUES TO CONVINCE PHYSICIANS TO PRESCRIBE AND PATIENTS TO USE OPIOIDS TO TREAT NON-MALIGNANT PAIN (NMP)

See **Exhibit B.360** hereto attached.

7.361 OPINION – THE NY-ATTORNEY GENERAL'S OFFICE DEMANDED THAT THE "VENTURE" REMOVE A MISLEADING CLAIM THAT "MOST DOCTORS" SUGGEST PATIENTS USUALLY DO NOT BECOME ADDICTED TO EXTENDED RELEASE OPIOIDS

See **Exhibit B.361** hereto attached.

7.362 OPINION – OPIOIDS INCREASE SENSITIVITY TO PAIN IN SOME PATIENTS

See **Exhibit B.362** hereto attached.

7.363 OPINION – THE OPIOID PMR CONSORTIUM (OPC) COMPOSITION

See **Exhibit B.363** hereto attached.

7.364 OPINIONS: THE SACKLER FAMILY ORIGINATED GHOSTWRITING AND THE USE OF MEDICAL JOURNALS AS MEDICAL MARKETING TOOLS TO INCREASE DRUG SALES. THIS PRACTICE HAS SINCE BEEN WIDELY ADOPTED BY THE PHARMACEUTICAL AND MEDICAL DEVICE INDUSTRY.

See **Exhibit B.364** hereto attached.

7.365 OPINION – THE VISUAL ANALOGUE SCALE IS NOT RELIABLE; THEREFORE, ALL PAIN STUDIES THAT USE IT ARE UNINTERPRETABLE.

See **Exhibit B.365** hereto attached.

7.366 OPINION – THERE ARE CULTURAL AND ETHNICAL DISPARITIES IN THE WAY INDIVIDUALS PERCEIVE AND EXPERIENCE PAIN.

See **Exhibit B.366** hereto attached.

7.367 OPINION – ADDICTION DEFINITION

See **Exhibit B.367** hereto attached.

7.368 OPINION – AMERICAN PAIN SOCIETY (APS), AMERICAN PAIN FOUNDATION (APF) AND OTHER PAIN SOCIETIES WERE FRONTS FOR THE "VENTURE". "UNCONDITIONAL GRANTS" WERE CONDITIONAL ON THE CONDITION THAT THE PAIN SOCIETIES DID THE "VENTURE'S" BIDDING.

See **Exhibit B.368** hereto attached.

7.369 OPINION – THE "VENTURE" ACTED IN CONCERT TO STRATEGICALLY UTILIZE THIRD PARTIES, INCLUDING BUT NOT LIMITED, TO FRONT GROUPS, KEY OPINION LEADERS, ADVOCACY GROUPS, UNBRANDED PROMOTION, PROFESSIONAL SOCIETIES, TRADE GROUPS AND COMPANY-SPONSORED NON-DRUG SPECIFIC PROMOTION, AND CONTINUING EDUCATION PROGRAMS, TO CREATE THE CONDITIONS NECESSARY TO CARRY OUT THE GOALS OF THE "VENTURE", OBSCURING THE "VENTURE'S" ROLE.

See **Exhibit B.369** hereto attached.

7.370 OPINION – WA SOUGHT TO AND DID CIRCUMVENT CARDINAL RED FLAG STORE SHIPMENTS.

See **Exhibit B.370** hereto attached.

7.371 OPINION – WALGREENS AND PURDUE HAD A REBATE PROGRAM THAT RELATED TO FORMULARY ACCESS AMONG OTHER THINGS.

See **Exhibit B.371** hereto attached.

7.372 OPINION – WALGREENS AUDITING WAS INADEQUATE.

See **Exhibit B.372** hereto attached.

7.373 OPINION – WALGREENS CREATED COMMUNICATIONS FOR PURDUE FOR DISTRIBUTION TO CUSTOMERS AND PHARMACISTS.

See **Exhibit B.373** hereto attached.

7.374 OPINION –WALGREENS SUSPICIOUS ORDER MONITORING WAS INADEQUATE.

See **Exhibit B.374** hereto attached.

7.375 OPINION – WALGREENS WAS A WHOLESALER TO ITSELF

See **Exhibit B.375** hereto attached.

7.376 OPINION – WALGREENS SYSTEMS COULD BE MANIPULATED TO ALLOW STORES TO CIRCUMVENT QUANTITY RESTRICTIONS - KNOWN ISSUE - 'THIS IS HOW THE SYSTEM ALWAYS WORKED'

See **Exhibit B.376** hereto attached.

7.377 OPINION – WHEN WALGREENS CIRCUMVENTED CARDINAL RED FLAGS THEY BOUGHT A LARGE STAKE IN AMERISOURCEBERGEN.

See **Exhibit B.377** hereto attached.

7.378 OPINION – WHOLESALERS PROMOTED DRUG USE.

See **Exhibit B.378** hereto attached.

7.379 OPINION – YALE FORMULARY IS VERY IMPORTANT.

See **Exhibit B.379** hereto attached.

7.380 OPINION – PURDUE TRAINED WALGREENS PHARMACISTS IN 1996

See **Exhibit B.380** hereto attached.

7.381 OPINION – "VENTURE" MEMBER JANSSEN MISREPRESENTED THE ADDICTION POTENTIAL OF OPIOIDS IN GENERAL AND ITS OPIOIDS IN PARTICULAR.

See **Exhibit B.381** hereto attached.

7.382 OPINION – THE "VENTURE" WORKED TOGETHER TO CREATE GHOST WRITTEN INDUSTRY EDITED PAPERS TO SUPPORT THEIR MARKETING.

See **Exhibit B.382** hereto attached.

7.383 OPINION: AS REQUESTED BY THE FDA, THE "VENTURE", WORKING AS THE "INDUSTRY WORKING GROUP," CREATED A DOCUMENT TO DEFINE "ABUSE", "ADDICTION" AND "OPIOID PSEUDO-ADDICTION" AND AID THE FDA IN THE CREATION OF THE RISK EVALUATION AND MITIGATION STRATEGY (REMS). THUS THE FDA PLACED THE CONVICTED CRIMINAL AND FDA RULE BREAKERS IN CHARGE OF THE CHICKENS.

See **Exhibit B.383** hereto attached.

7.384 OPINION – THE "VENTURE" HAS FALSELY STATED THAT PATIENTS WILL NOT BECOME ADDICTED IF PATIENTS ARE TAKING OPIOIDS FOR LEGITIMATE, "MEDICAL PURPOSES."

See **Exhibit B.384** hereto attached.

7.385 OPINION – ACTAVIS HAD MARKETING AGREEMENTS WITH SOME DISTRIBUTORS AND PROVIDED MCKESSON WITH "TALKING POINTS" TO SELL OXYMORPHONE TO PHARMACISTS.

See **Exhibit B.385** hereto attached.

7.386 OPINION – THE "VENTURE" DID NOT INCLUDE FDA-MANDATED DRUG LABEL WARNINGS IN THE PHYSICIAN'S DESK REFERENCE (PDR) FOR ALL OF THEIR DRUGS THEY SOLD FOR EVERY YEAR THAT THEY WERE SOLD. THE "VENTURE" MEMBERS HAD A DUTY TO ENSURE THAT DOCTORS RECEIVED THESE WARNINGS. WITHOUT INCLUSION IN THE PDR, MANY DOCTORS DID NOT RECEIVE THE FDA-MANDATED WARNING LABELS.

See **Exhibit B.386** hereto attached.

7.387 OPINION: PLANNING COMMITTEE MEMBERS, TEACHERS/PRESENTERS, AND AUTHORS OF CME SHOULD DISCLOSE RELATIONSHIPS WITH COMMERCIAL INTERESTS.

See **Exhibit B.387** hereto attached.

7.388 OPINION – PURDUE USED THE 2001 LABEL CHANGE TO EXPAND THE TARGET MARKET. ALL SIMILAR OPIOID LABELS CHANGED AT THE SAME TIME.

See **Exhibit B.388** hereto attached.

7.389 OPINION – OPIOIDS HAVE PARADOXICAL EFFECTS ON PAIN INCREASING PAIN IN SOME PATIENTS. IT CAN BE DIFFICULT (PERHAPS IMPOSSIBLE IN A STUDY) TO DISTINGUISH TOLERANCE AND HYPERALGESIA, AND IT IMPOSSIBLE TO DO SO SOLELY BASED ON THE CLINICAL OBSERVATION OF THE PATIENT. THIS IS NOT ACCOUNTED FOR IN ANY PAIN OPIOID STUDIES. AS A RESULT THE VALIDITY OF ALL THESE STUDIES IS QUESTIONABLE. THIS IS ANOTHER REASON THAT ENRICHED ENROLMENT WITH RANDOMISED WITHDRAWAL (EERW) STUDY DESIGN IS INVALID AND THAT THE FDA VIEW THAT "WE KNOW [OPIOIDS] WORK" IS NONSENSE

See **Exhibit B.389** hereto attached.

7.390 OPINION: THE "VENTURE" MARKETED GENERIC DRUGS, SPECIFICALLY TARGETING HIGH PRESCRIBING PHYSICIANS TO "INCREASE THEIR SCRIPTS." THIS INCLUDES PHYSICIANS WHO ARE OVERLY AND INAPPROPRIATELY PRESCRIBING DRUGS.

See **Exhibit B.390** hereto attached.

7.391 OPINION: THE FDA NEVER APPROVED OXYCONTIN AS A TREATMENT FOR CHRONIC PAIN.

See **Exhibit B.391** hereto attached.

7.392 OPINION: THE FDA ONLY APPROVED OXYCONTIN FOR USE BY TREATERS WHO WERE "KNOWLEDGEABLE IN THE USE OF POTENT OPIOIDS FOR THE MANAGEMENT OF CHRONIC PAIN."

See **Exhibit B.392** hereto attached.

7.393 OPINION – DR. ROBERT RAPPAPORT WAS CAPTURED BY INDUSTRY AND COORDINATED WITH THE "VENTURE" TO INCREASE OPIOID USE, EASE OPIOID APPROVALS, EXPAND OPIOID INDICATIONS AND MINIMIZE ADDICTION RISK.

See **Exhibit B.393** hereto attached.

7.394 OPINION – THIS IS AN OVERVIEW OF THE US DISTRIBUTION AND REIMBURSEMENT SYSTEM FOR OUTPATIENT DRUGS

See **Exhibit B.394** hereto attached.

7.395 OPINION –WALGREENS SYSTEMS COULD BE MANIPULATED TO ALLOW STORES TO CIRCUMVENT QUANTITY RESTRICTIONS. THIS WAS A KNOWN ISSUE. "[T]HIS IS HOW THE SYSTEM ALWAYS WORKED"

See **Exhibit B.395** hereto attached.

7.396 OPINION – "VENTURE" KEY OPINION LEADERS (KOLS) CREATED POORLY SUPPORTED MEDICAL LITERATURE TO SUPPORT CLAIMS THAT WOULD EXPAND THE MARKET FOR OPIOIDS.

See **Exhibit B.396** hereto attached.

7.397 OPINION – AROUND 1997, "VENTURE" MEMBERS ORTHO-MCNEIL (JOHNSON & JOHNSON) AND PURDUE BEGAN CO-PROMOTING ULTRAM SR, INTENDED FOR THE USE OF MORE MODERATE PAIN.

See **Exhibit B.397** hereto attached.

7.398 OPINION –CEPHALON'S ACTIQ WAS NOT INDICATED FOR, BUT WAS MARKETED OFF LABEL FOR MINOR PAIN.

See **Exhibit B.398** hereto attached.

7.399 OPINION – THE "VENTURE" AGREE NOT TO COMPETE ON SAFETY.

See **Exhibit B.399** hereto attached.

7.400 OPINION – DEA CITED WALGREENS FOR BAD PRACTICES AT PERRYSBURG DISTRIBUTION CENTER.

See **Exhibit B.400** hereto attached.

7.401 OPINION – DICTIONARY OF TERMS FROM WHOLESALER AGREEMENTS.

See **Exhibit B.401** hereto attached.

7.402 OPINION – WHOLESALER CONNECTIONS TO PHARMACIES.

See **Exhibit B.402** hereto attached.

7.403 POSSIBLE LIMITATIONS TO MY ANALYSIS.

See **Exhibit B.403** hereto attached.

7.404 OPINION – THE "VENTURE" ACTED IN CONCERT TO:

See **Exhibit B.404** hereto attached.

7.405 OPINION – THE "VENTURE" RECOGNIZED THAT THERE WAS NO EVIDENCE THAT OPIOIDS WERE INDICATED FOR THE TREATMENT OF CHRONIC NON-MALIGNANT PAIN.

See **Exhibit B.405** hereto attached.

7.406 OPINION – WHOLESALE DISTRIBUTORS ALSO OWN AND OPERATE SPECIALTY PHARMACIES.

See **Exhibit B.406** hereto attached.

7.407 OPINION – PRESCRIPTION OPIOIDS CAUSED THE OPIOID CRISIS.

See **Exhibit B.407** hereto attached.

7.408 OPINION – DOCTORS ON THE "VENTURE'S" PAYROLL ADMITTED THAT PSEUDOADDICTION DESCRIBES BEHAVIORS 'CLEARLY CHARACTERIZED AS DRUG ABUSE' AND PUT THE "VENTURE" AT RISK OF 'SANCTIONING ABUSE.'

See **Exhibit B.408** hereto attached.

7.409 OPINION – PURDUE CLAIMED OXYCONTIN CR WAS APPROVED FOR POST-OPERATIVE PAIN. THIS IS NOT TRUE.

See **Exhibit B.409** hereto attached.

7.410 OPINION – PURDUE DID NOT REMOVE THE 160 MG DOSE FORM THE LABEL UNTIL 2011 ALTHOUGH IT WAS AWARE OF THE FACT THAT ITS RISKS OUTWEIGHED BENEFITS BY 2001.

See **Exhibit B.410** hereto attached.

7.411 OPINION – PURDUE EDITED THE AMERICAN MEDICAL DIRECTORS ASSOCIATIONS GUIDELINE FOR CHRONIC PAIN MANAGEMENT IN THE LONG-TERM CARE SETTING.

See **Exhibit B.411** hereto attached.

7.412 OPINION – PURDUE STOPPED SELLING THE 160 MG PILL BECAUSE IT WAS NOT SAFE AND EFFICACIOUS BUT NEVER DID A RECALL.

See **Exhibit B.412** hereto attached.

7.413 OPINION – THE "VENTURE" - ROXANE (NOW MALLINCKRODT) INCLUDING DISTRIBUTORS MARKETED UNAPPROVED DRUGS.

See **Exhibit B.413** hereto attached.

7.414 OPINION – OUT THE DRUGS TARGETED FOR GOOD FAITH DISPENSING (GFD), ONLY THE USE RATES OF OXYCONTIN WERE AFFECTED.

See **Exhibit B.414** hereto attached.

7.415 OPINION – THE "VENTURE" CONTINUALLY REMINDED ITS STAFF THAT SHIFTS TO LOWER DOSES WOULD RESULT IN HUGE MONETARY LOSSES FOR THE "VENTURE".

See **Exhibit B.415** hereto attached.

7.416 OPINION – THE "VENTURE" USED A VARIETY OF SALES TECHNIQUES TO CONVINCE PHYSICIANS TO PRESCRIBE AND PATIENTS TO USE OPIOIDS TO TREAT CHRONIC NON-MALIGNANT PAIN.

See **Exhibit B.416** hereto attached.

7.417 OPINION – THE "VENTURE" SEEDED THE LITERATURE TO INCREASE USE OF OPIOIDS IN MINORITY POPULATIONS.

See **Exhibit B.417** hereto attached.

7.418 OPINION – THE "VENTURE" SHARED INFORMATION.

See **Exhibit B.418** hereto attached.

7.419 OPINION – THE "VENTURE" SHOULD HAVE TRAINED DOCTORS TO TELL PATIENTS WHAT TO DO WITH EXTRA PILLS AND HOW TO PROPERLY DISPOSE OF THEM. THIS SHOULD BE IN THE PACKAGE INSERT.

See **Exhibit B.419** hereto attached.

7.420 OPINION – THE "VENTURE" USED SEX TO SELL PRODUCT – INSYS.

See **Exhibit B.420** hereto attached.

7.421 OPINION – THE VISUAL ANALOGUE SCALE IS NOT RELIABLE AND THEREFORE ALL PAIN STUDIES THAT USE IT ARE UNINTERPRETABLE.

See **Exhibit B.421** hereto attached.

7.422 OPINION – VIP = VOLUME INCENTIVE PROGRAM (PRICING SELL MORE GET INCREASED IN REBATE). THIS IS AN EXAMPLE OF THE "VENTURE" IN OPERATION. OXY DRIVES SALES MALLINCKRODT AND WALGREENS.

See **Exhibit B.422** hereto attached.

7.423 OPINION – WALGREENS AGREED TO CREATE "COMMUNICATIONS" ON HYSINGLA.

See **Exhibit B.423** hereto attached.

7.424 OPINION – WALGREENS AND MALLINCKRODT WORKED TOGETHER ON SUSPICIOUS ORDER MONITORING (SOM) FAILURE IS JOINT RESPONSIBILITY.

See **Exhibit B.424** hereto attached.

7.425 OPINION – WHOLESALERS CONTROLLED ENTIRE CHAINS OR PHARMACY OPIOID USE AND HAD A SWITCH PROGRAM.

See **Exhibit B.425** hereto attached.

7.426 OPINION – ALLERGAN DEFINED "CLOSED FORMULARY" AND "INCENTIVE FORMULARY" AS FOLLOWS:

See **Exhibit B.426** hereto attached.

7.427 OPINION – ENDO WAS EITHER TOO CHEAP TO ADD ITS OPIOID LABELS TO THE 2014 PDR OR COMPLETELY IRRESPONSIBLE FOR THIS FAILURE TO WARN LEARNED INTERMEDIARIES OF ANY DATA CONCERNING THESE DANGEROUS DRUGS.

See **Exhibit B.427** hereto attached.

7.428 OPINION – "VENTURE" FUNDED PAPER AND CME ARE BIASED TO INCREASE OPIOID USE.

See **Exhibit B.428** hereto attached.

7.429 OPINION – MARKETING HAS A RETURN ON INVESTMENT (ROI) AND INFLUENCES DOCTORS.

See **Exhibit B.429** hereto attached.

7.430 OPINION – MCKESSON HAD MARKETING AGREEMENTS WITH MALLINCKRODT, PURDUE AND TEVA.

See **Exhibit B.430** hereto attached.

7.431 OPINION – WHOLESALERS WORKED IN CONCERT WITH MANUFACTURERS TO PROMOTE OPIOID USE THROUGH PHARMACIES.

See **Exhibit B.431** hereto attached.

7.432 OPINION – LABEL CHANGES ON ABUSE POTENTIAL CHANGES OVER TIME

See **Exhibit B.432** hereto attached.

7.433 OPINION – THE "VENTURE" MISLED PRESCRIBERS ABOUT THE POTENCY OF OXYCONTIN. THE "VENTURE" TARGETED NON-CANCER PATIENTS TO INCREASE MARKET SIZE TO INAPPROPRIATE PATIENTS. THE "VENTURE" TARGETED NON-CANCER PATIENTS TO MISLEAD PRESCRIBERS ABOUT THE POTENCY AND THUS ADDICTION POTENTIAL OF OXYCONTIN.

See **Exhibit B.433** hereto attached.

7.434 OPINION – PURDUE RECOMMENDED USING OXYCONTIN FOR SHINGLES. THIS IS AN EFFORT TO INCREASE PROFITS BY ENCOURAGING USE IN DISEASE IT WAS NOT INDICATED FOR.

See **Exhibit B.434** hereto attached.

7.435 OPINION – PURDUE WAS AWARE OF THE FACT THAT DOCTORS WERE NOT AWARE OF THE POTENCY OF OXYCONTIN. INSTEAD OF CORRECTING THIS MISIMPRESSION, PURDUE CAPITALIZED ON IT TO INCREASE OXYCONTIN USE.

See **Exhibit B.435** hereto attached.

7.436 OPINION – THE "VENTURE" INFLUENCED WHO GUIDELINES AND THEN USED THEM TO UP SELL.

See **Exhibit B.436** hereto attached.

7.437 OPINION – THE CLINICAL STUDIES CITED IN OPIOID DRUG LABELS CHANGED OVER TIME.

See **Exhibit B.437** hereto attached.

7.438 OPINION: THE "VENTURE" USED THE AMERICAN PAIN FOUNDATION AND INDUSTRY FUNDED KEY OPINION LEADERS (KOLS) TO CREATE LITERATURE FOR THE PURPOSE OF INFLUENCING POLICY MAKERS AND REPORTERS AND FAILED TO DISCLOSE ALL OF THE INDUSTRY CONNECTIONS OF THE KOLS.

See **Exhibit B.438** hereto attached.

7.439 OPINION – THE PAIN CARE FORUM (PCF) WAS MADE UP OF THE FOLLOWING MEMBERS AND WAS HELD AT THE OFFICE OF POWERS, PYLES, SUTTER & VERVILLE A WASHINGTON DC ATTORNEY'S OFFICE.

See **Exhibit B.439** hereto attached.

7.440 OPINION – THIRD PARTY ENDORSEMENTS ARE MORE EFFECTIVE AT INFLUENCING BEHAVIOR THAN FIRST PARTY ENDORSEMENTS. IN ADDITION, THESE THIRD-PARTY ENDORSEMENTS TARGETED CONSUMERS AND CIRCUMVENTED LEARNED INTERMEDIARY PHYSICIANS. THE COMPANIES DID NOT INCLUDE APPROPRIATE WARNINGS AND CAUTIONS IN THEIR ENDORSEMENTS TO CONSUMERS.

See **Exhibit B.440** hereto attached.

7.441 OPINION – "VENTURE" MEMBERS PURDUE AND JANSSEN WORKED TOGETHER TO INCREASE OPIOID USE.

See **Exhibit B.441** hereto attached.

7.442 OPINION – THE "VENTURE" MEMBERS SHARED KEY OPINION LEADERS (KOLS) PORTENOY, CARR.

See **Exhibit B.442** hereto attached.

7.443 OPINION – ROBERT WOOD JOHNSON FOUNDATION (RWJF) ASSISTED THE "VENTURE".

See **Exhibit B.443** hereto attached.

7.444 OPINION – ALLERGAN DID MANY BAD THINGS, SUCH AS LYING ABOUT ADDICTION, EXPANDING THE OPIOID MARKET, CLAIMED PAIN WAS A DISEASE, AND ENTERED INTO SETTLEMENTS AND GUILTY PLEAS.

See **Exhibit B.444** hereto attached.

7.445 OPINION – MALLINCKRODT KNEW THEY WERE FEEDING ADDICTS. THEY THOUGHT THIS WAS FUNNY. I DISAGREE.

See **Exhibit B.445** hereto attached.

7.446 OPINION – THE "VENTURE" USED FORMULARIES TO EXPAND THE OPIOID MARKET.

See **Exhibit B.446** hereto attached.

7.447 OPINION: THE "VENTURE" ENGAGED IN CONCERTED ACTION TO INCREASE SALES BY MINIMIZING ADDITION RISK, ENCOURAGING OVERUSE, ENCOURAGING USE BY PHYSICIANS WHO THE BLACK BOX WARNING SAID SHOULD NOT USE OPIOIDS.

See **Exhibit B.447** hereto attached.

7.448 OPINION – THE INDICATIONS FOR THE "VENTURE'S" OPIOID MEDICATIONS CHANGED OVER TIME.

See **Exhibit B.448** hereto attached.

7.449 OPINION – THE DOSAGE FORMS AND STRENGTHS LISTED ON THE "VENTURE'S" OPIOID MEDICATION LABELS CHANGED OVER TIME.

See **Exhibit B.449** hereto attached.

7.450 OPINION – THE BLACK BOX WARNINGS FOR THE "VENTURE'S" OPIOID MEDICATIONS CHANGED OVER TIME.

See **Exhibit B.450** hereto attached.

7.451 OPINION: THE "VENTURE" CREATED AND SUPPORTS THE USE OF THE ENRICHED ENROLLMENT RANDOMIZED WITHDRAWAL (EERW) STUDY DESIGN FOR APPROVING ANALGESICS FOR CHRONIC NON-CANCER PAIN. AS OF 2016, 5 DRUGS HAVE BEEN APPROVED FOR CHRONIC PAIN ON THE BASIS OF EERW STUDIES. EERW IS FLAWED METHODOLOGY.

See **Exhibit B.451** hereto attached.

7.452 OPINION – PURDUE WAS AWARE OF THE FACT THAT PATIENTS WERE ILLEGALLY OBTAINING OPIOIDS UNDER MY NAME. IT FAILED TO REPORT THIS. THIS METHOD COULD HAVE BEEN USED TO TRACK DIVERSION IN GENERAL.

See **Exhibit B.452** hereto attached.

7.453 OPINION – OHIO MEDICAID DEPENDED ON THE PHARMACY BENEFIT MANAGERS (PBMS) FOR FORMULARY DRUG SELECTION.

See **Exhibit B.453** hereto attached.

7.454 OPINION – TEVA USED ITS HOTLINE TO OFF LABEL MARKET.

See **Exhibit B.454** hereto attached.

7.455 OPINION – ALL THESE OPIOIDS HAD THE SAME RISK OF ADDICTION FOR THE SAME EFFECTIVE DOSE AND THE WARNINGS SHOULD HAVE AT A MINIMUM BEEN THE STRONGEST THAT WAS APPROVED FOR ANY OF THEM.

See **Exhibit B.455** hereto attached.

7.456 OPINION: THE FDA NEVER APPROVED OXYCONTIN AS A TREATMENT FOR CHRONIC PAIN.

See **Exhibit B.456** hereto attached.

7.457 OPINION – THE CLINICAL STUDIES ON THE "VENTURE'S" OPIOID DRUG LABELS CHANGED OVER TIME.

See **Exhibit B.457** hereto attached.

7.458 OPINION – THE "VENTURE" MEMBERS USED VARIOUS METHODS TO PUSH DRUGS - FORMULARY ACCESS WAS KEY.

See **Exhibit B.458** hereto attached.

7.459 OPINION – WALGREENS CIRCUMVENTED THE DEA SETTLEMENT.

See **Exhibit B.459** hereto attached.

7.460 OPINION – PURDUE RESISTED IMPROVEMENTS IN SUSPICIOUS ORDER MONITORING.

See **Exhibit B.460** hereto attached.

7.461 OPINION – WALGREEN'S SOM WAS A JOKE.

See **Exhibit B.461** hereto attached.

7.462 OPINION – THIS IS THE TIMELINE OF FDA ACTIVITY THAT FDA CREATED OF ITS ACTIVITY RELATED TO OPIOID ADDICTION – IT OMITS REGULATORY CAPTURE.

See **Exhibit B.462** hereto attached.

7.463 OPINION – THE "VENTURE" GHOST WROTE THE REVIEW OF ENRICHED ENROLLMENT RANDOMIZED WITHDRAWAL (EERW) STUDIES. THIS IS UNETHICAL AND ALTERED THE PAPER IN A MATERIAL WAY TO MAKE IT APPEAR THAT EERW STUDIES ARE LEGITIMATE WHEN THEY ARE NOT.

See **Exhibit B.463** hereto attached.

7.464 OPINION – THE "VENTURE" USED DISCOUNT CARDS TO INCREASE SALES

See **Exhibit B.464** hereto attached.

7.465 OPINION – PURDUE HAD AN EXTENSIVE MARKETING PROGRAM FOR HOSPITAL FORMULARY ACCESS.

See **Exhibit B.465** hereto attached.

7.466 OPINION – PURDUE SPOLIATED DOCUMENTS AND HARD DRIVES.

See **Exhibit B.466** hereto attached.

7.467 OPINION – THIS IS A PLACED AD THAT APPEARS TO BE A MEDICAL ARTICLE THAT WAS GHOST WRITTEN FOR A KEY OPINION LEADER (KOL) WHO DID NOT DISCLOSE HIS CONFLICTS.

See **Exhibit B.467** hereto attached.

7.468 OPINION – MCKESSON BLAMES MANUFACTURERS AND AVOIDS ITS OWN RESPONSIBILITY.

See **Exhibit B.468** hereto attached.

7.469 OPINION – THIS DESCRIBES PHARMACEUTICAL PRICING AND PHARMACY BENEFIT MANAGER (PBM) AND MANUFACTURING MANIPULATION OF THE SYSTEM TO INFLUENCE DRUG USE.

See **Exhibit B.469** hereto attached.

7.470 OPINION – THIS IS PURDUE'S AND THE INDUSTRY'S PRODUCT DISTRIBUTION METHODOLOGY.

See **Exhibit B.470** hereto attached.

7.471 OPINION – THE POST MARKETING STUDIES WERE DONE BY THE "VENTURE" AS A WHOLE. THIS IS AN EXAMPLE OF REGULATORY CAPTURE. NO RATIONAL REGULATORY AGENCY WOULD INVITE CONVICTED CRIMINALS TO CONDUCT STUDIES ON THEIR OWN PRODUCTS. INDUSTRY HELPED CREATE OR ACTUALLY PERFORM THE FISHBAIN STUDY.

See **Exhibit B.471** hereto attached.

7.472 OPINION – J&J MARKETED NARCOTICS TO INAPPROPRIATE PATIENTS.

See **Exhibit B.472** hereto attached.

7.473 OPINION – DEFINITION – INSTEAD OF NAMING PARTICULAR COMPANIES IN MY OPINIONS, I REFER TO MANUFACTURING AND DISTRIBUTOR DEFENDANTS (INCLUDING THEIR ASSOCIATED INDIVIDUALS AND/OR ORGANIZATIONS) AS THE "VENTURE".

See **Exhibit B.473** hereto attached.

7.474 OPINION – THE BOARDS OF J&J AND RWJF OVERLAP. IT IS IMPROPER FOR A NON-PROFIT TO DO SOMETHING THAT BENEFITS A BOARD MEMBER'S COMPANY.

See **Exhibit B.474** hereto attached.

7.475 OPINION – THE "VENTURE" USED AND CONTROLLED MANY FRONT GROUPS TO UNDERMINE ADDICTION RISK AND INCREASE MARKET TO INAPPROPRIATE PATIENTS

See **Exhibit B.475** hereto attached.

7.476 OPINION – MALINCKRODT OPINIONS

See **Exhibit B.476** hereto attached.

7.477 OPINION – "VENTURE" MEMBERS HAD AGREEMENTS WITH WHOLESALERS, INCLUDING BUT NOT LIMITED TO: "

See **Exhibit B.474** hereto attached.

7.478 OPINION – "VENTURE" MEMBERS HAD INVENTORY LICENSE AGREEMENTS WITH WALGREENS WHEREBY THEY RECEIVED DATA THAT COULD HAVE BEEN USED TO MONITOR SUSPICIOUS ORDERS. THIS DATA GAVE VENTURE MEMBERS VISIBILITY INTO THEIR CUSTOMER'S CUSTOMERS.

See **Exhibit B.478** hereto attached.

7.479 OPINION – CVS'S SUSPICIOUS ORDER MONITORING SYSTEM DID NOT MONITOR SUSPICIOUS ORDERS. IT'S SOM POLICY SPECIFIED THAT IF MULTIPLE ORDERS FOR THE SAME STORE ARE FLAGGED DURING THE SAME MONTH, ALL ORDERS AFTER THE FIRST ORDER WILL NOT BE INVESTIGATED AND WILL BE AUTOMATICALLY RELEASED BASED ON THE RELEASE OF THE FIRST ORDER

See **Exhibit B.479** hereto attached.

7.480 OPINION – WALMART HELPED ACTAVIS MARKET OPIOIDS

See **Exhibit B.480** hereto attached.

7.481 OPINION – THE GAO DOCUMENTED BAD CONDUCT BY PURDUE THAT INCREASED ADDICTION

See **Exhibit B.481** hereto attached.

7.482 OPINION – CARDINAL DELIVERED MANUFACTURERS MARKETING MESSAGES TO CVS

See **Exhibit B.482** hereto attached.

7.483 OPINION – OPIOIDS ARE NEVER MENTIONED AS AN OPTION FOR RX OF RHEUMATOID ARTHRITIS.

See **Exhibit B.483** hereto attached.

7.484 OPINION – OPIOIDS ARE NOT RECOMMENDED FOR RX OF OSTEOARTHRITIS

See **Exhibit B.484** hereto attached.

7.485 OPINION – OPIOIDS SHOULD NOT BE USED FOR LOW BACK PAIN. CHRONIC OPIOIDS ARE VERBOTEN.

See **Exhibit B.485** hereto attached.

7.486 OPINION – OPIOIDS ARE NOT TREATMENT FOR FIBROMYALGIA

See **Exhibit B.486** hereto attached.

7.487 OPINION – RITE AID PROVIDED MARKETING SERVICES TO TEVA

See **Exhibit B.487** hereto attached.

7.488 OPINION – THESE ARE THE MEMBERS OF THE "VENTURE"

See **Exhibit B.488** hereto attached.

7.489 OPINION – MEMBERS OF THE "VENTURE" ENTERED AGREEMENTS WITH THE DEA AND DOJ FOR VIOLATING THE LAW

See **Exhibit B.489** hereto attached.

8 LIMITATIONS

Limitations to my analysis include:

1) I could not review missing or destroyed documents
2) I could not review documents withheld as non-responsive
3) I could not review documents withheld as privileged
4) I could not review redacted language
5) I did not review correspondence in non-produced personal emails
6) I did not review correspondence in non-produced text messages
7) Multiple productions remain incomplete
8) I do not have access to all of the documents produced in other state specific litigation.
9) Monitoring reports under Corporate Integrity Agreements were not produced
10) Ethics Hotline reports under Corporate Integrity Agreements were not produced

See **Exhibit B.403** hereto attached.

9 FACTS AND DATA REVIEWED, READ OR CONSIDERED

Production is ongoing, and I reserve the right to supplement this list as more documents become available.

I have reviewed, read or considered:

1) The published medical literature[60] on Opioids, Pain, Addiction, Pain Treatments, NSAIDs. See **Exhibit C**.
2) Documents and metadata produced by the Defendants, Plaintiffs, and Third Parties specifically referenced in **Exhibit D** hereto attached.
3) Legal complaints filed against opioid manufacturers and distributers in Massachusetts and Florida.
4) The Master Amended Complaint filed in this case (Opiate MDL).
5) Deposition transcripts (with exhibits) taken in this case (Opiate MDL).
6) Other historical deposition transcripts (including Covington and Fishbain) taken in prior Purdue litigation.
7) Articles published in magazines and newspapers referenced in Opinions.
8) Websites (including government sites) referenced in Opinions.
9) News media publications referenced in Opinions.
10) 1984-2017 Editions of the Physician's Desk Reference.

It is my expectation that I will review the Expert Reports of Plaintiffs' and Defendants' Experts once they are made available.

It is my understanding that production is ongoing. Should documents be produced, I reserve the right to supplement my opinions.

[60] Every attempt was made to include literature cited in this report and to the extent a piece of literature was missed, it is incorporated herein.

10 PRIOR EXPERT TESTIMONY

- **2015**
  - *Anderson et al v. Aldrich Chemical Company et al.*, Docket No. 2009CV003457 (Wi Cir. Ct.)
  - *Smead v. Chr. Hansen Inc. et al.*, Docket No. 2009CV003112 (Wis Cir. Ct.)
  - *Boyd v. Ameron International Corporation, et al.*, Docket No. RG14738647 (Cal.Super.)
  - *Norful vs Cooper Bussmann*, Docket No. 1222-CC00961 (Mo. Cir. Ct.)
  - *Solorzano v. Honeywell*, Docket No. GD-15-008069 (PA Ct. Comm. Pleas)
  - Emerson v. *Union Pacific*, Docket No. RG-13698637 (Cal.Super.)
  - *Trejo v. Hyster et al.*, Docket No. BC574146 (Cal.Super.)
  - *Aoki v. DePuy, et al.*, Docket No. 3-13-cv-1071-K, MDL No. 2244 (U.S.D.C. N.D. TX)
- **2016**
  - *Amesquita et al v. Gilster-Mary Lee, et al.*, Docket No. ED 99266 (MO Ct. App., E. Dist.)
  - *Jo Levitt vs. Merck*, Docket No. 06–CV–00818–W–DW (U.S.D.C. W.D. MO)
  - *Crawford v. Gold Coast*, Docket No. 13-EV-017885-B (Fulton County, GA)
  - *Tyler vs. American Optical, et al.*, Docket No. LA CV16-02337 JAK (ASx) (U.S.D.C. C.D. CA)
  - *Ortwein vs. CertainTeed*, Docket No. RG13701633 (Cal.Super.)
  - *Olson vs. Metalclad*, Docket No. A102605 (Cal. App.)
- **2017**
  - *Wurster v. The Plastics Group, Inc.*, Docket No. 4-14-cv-503-CRW-SBJ (U.S.D.C. S.D. Iowa)
  - *Zampa v. v. Georgia-Pacific LLC, et al.*, Docket No. RG16836998 (Cal.Super.)
  - *Williams v. UCC*, Docket No. 16-CI-1842 (Ky. Cir. Ct.)
  - *Darpel v. Cargill Flavors,* Docket No. 12-CI-446 (Ky. Cir. Ct.)
- **2018**
  - *Leavitt v. Johnson and Johnson, et al.*, Docket No. RG1782401 (Cal.Super.)
  - *Ingham v. Johnson & Johnson, et al.*, Docket No. 4:17–CV–1857 SNLJ (U.S.D.C. E.D. MO)
  - *Cynthia Hayes, as Executrix of the Estate of Donna Ann Hayes v. J& J*, Docket No. 16-CI-03503 (Ky. Cir. Ct.)
  - *In re NCAA*, Docket No. 05-17-00951-CV, 543 S.W.3d 487 (Tex. Ct. App.)
  - *Thompson v. Air & Liquid Systems Corp., et al.*, Docket No. 18-2-05736-7 (Wash.Super.)
- **2019**
  - Fong v. Johnson and Johnson, et al., Docket No. 2:18-CV-00470 (U.S.D.C. C.D. CA)

11 COMPENSATION

My billing rate in this litigation is $650 per hour for depositions and $600 per hour for trial testimony and preparation.

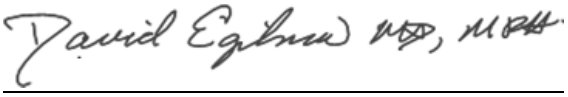
12SIGNATURE

RESERVATION OF RIGHTS

This report is a statement of opinions I expect to express in this matter and the basis and reasons for those opinions. This report summarizes only my current opinions and analyses to date, which are subject to change depending upon ongoing discovery and additional information. I respectfully reserve the right to supplement my report in light of this and any other additional fact discovery, opinions by other experts, and/or trial testimony. I also respectfully reserve the right to provide rebuttal opinions and testimony in response to other experts, and rebuttal testimony in response to any fact witnesses. In connection with my anticipated trial testimony in this action, I may use as exhibits various documents produced in this litigation that refer to or relate to the matters discussed in this report. In addition, i respectfully reserve the right to use animations, demonstratives, enlargements of actual attachments, and other information in order to convey my opinions.

I understand that i may be asked to provide further opinions and analyses on other issues, including in response to analyses provided by other experts. I will do so at the appropriate time set by the court.

Executed on this 25th day of March, 2019, in Attelboro, MA.



Report of David S. Egilman, MD, MPH

March 25, 2019 in Opiate MDL Litigation (MDL 2804)

This document exceeds the maximum permitted file size for upload onto the Electronic Court Filing system. Consequently, the balance of this document will be manually filed with the Court.